IN THE UNITED STATED DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

AMERITOX, LTD., and U.D. TESTING, INC.,	)	
	)	
Plaintiffs,	)	No. 08 C 4513
v.	)	
	)	Honorable Marvin E. Aspen
AEGIS SCIENCES CORP.,	)	
	)	
Defendant.	)	

AEGIS SCIENCES CORP.'S
RESPONSE IN OPPOSITION TO MOTION TO QUASH

Aegis Sciences Corp. ("Aegis") respectfully submits this response to the Motion to Quash Defendant's Subpoena of Sterling Partners filed by Sterling Partners. A copy of the subpoena at issue (the "Sterling Subpoena") is attached hereto as Exhibit A.

Without any prior attempt to confer with opposing counsel in order to seek resolution prior to bringing a discovery dispute motion to the Court, Sterling Partners asserts that the Sterling Subpoena should be quashed because (a) Sterling Partners allegedly cannot determine who issued the subpoena; (b) the subpoena seeks highly confidential material; and (c) it is unduly burdensome. The first argument is without merit given the fact that Sterling Partners was able to serve its Motion to Quash on Chicago attorney John D. Burke, who in fact, signed the subpoena. The second argument is equally lacking in merit. Sterling Partners' own law firm (also representing Ameritox) submitted a protective order in the underlying litigation that applies to third parties, and Sterling Partners offers no legitimate arguments to support its blanket assertion of confidentiality. Lastly, Sterling Partners' blanket assertions of undue burden are also baseless and unsupported by any facts. The requests in the subpoena are directly relevant to the underlying litigation, and Sterling Partners is the financial backer of the plaintiff, Ameritox, Ltd. ("Ameritox"), and by no coincidence, they are represented by the same law firm.

I. INTRODUCTION

The parties to the underlying litigation, Aegis and Ameritox, are clinical labs that perform drug testing. Ameritox sued Aegis in Florida federal court (referred to herein as the "Florida Litigation") alleging that Aegis was infringing on its patented methodology for determining whether patients were complying their dosage prescriptions for medication. Aegis also provides compliance testing, but does not use Ameritox's methodology, which Aegis asserts is junk science. Ameritox knew or should have known that Aegis was not using its methodology, and, in fact, after the Florida Lawsuit was pending for almost a year, Ameritox abandoned its patent infringement claims and acknowledged that there was no patent infringement.

Aegis asserts in the Florida Lawsuit that Ameritox has used the Florida Lawsuit to disparage Aegis and to cause harm to Aegis. Accordingly, Aegis has asserted claims against Ameritox for the wrongful prosecution of the Florida Lawsuit under various legal theories and defenses, including unclean hands, unfair competition, patent misuse and violation of anti trust laws for filing sham litigation.

Sterling Partners, based in the Chicago area, is the financial backer of Ameritox. It is highly unlikely that no one knows more about Ameritox's business and strategies than Sterling Partners. It is reasonably likely that Sterling Partners has information relating to the market position of Ameritox, and it is also likely that Sterling Partners is privy to communications with Ameritox related to this litigation as well as Ameritox's attempts to unfairly compete with Aegis as well as other competitors. It is also likely that Sterling Partners has documents that Ameritox has lost or destroyed. Sterling Partners may have also conducted its own investigation with respect to these matters and generated its own relevant documents. For this reason, Aegis served

the Sterling Subpoena on Sterling Partners to seek information that directly relates to its claims against Ameritox.

II. BACKGROUND

A. The Florida Litigation

1. The Allegations In The Florida Complaint And Counterclaim As Amended.

This subpoena arises out of a case pending in the United States District Court for the Southern District of Florida, styled *Ameritox, Ltd. And U.D. Testing, Inc. v. Aegis Sciences Corp.*, Case No. 08-CV-4513 (the "Florida Litigation") which was commenced by Ameritox on June 11, 2007. In its initial complaint in the Florida Litigation, Ameritox asserted that Aegis had infringed upon US. Patent Nos. 5,908,788 and 6,124,136 (the "Ameritox Patents"). Ameritox subsequently amended the initial complaint and added claims under the Florida Deceptive and Unfair Trade Practices Act; Tortious Interference with Business Relationships; Fraudulent Misrepresentation; and False Marking. A copy of Ameritox's amended complaint (the "Florida Complaint") entered January 25, 2008 (filed December 21, 2007) is attached hereto (without exhibits) as Exhibit B.

As is evidenced by the Florida Complaint, Ameritox is represented in the Florida Litigation by the Chicago firm, Bell, Boyd & Lloyd, LLP, which is the same law firm that is representing Sterling Partners in this proceeding.

Aegis answered Ameritox's Complaint and filed counterclaims alleging non-infringement and invalidity of the Ameritox Patents, Commercial Disparagement under the Lanham Act, Injurious Falsehood/Unfair Competition, Violation of the Florida Deceptive and Unfair Trade Practices Act; and Sham Litigation Violation of Sherman Anti Trust Act § 2. In its Affirmative Defenses, Aegis asserted that Aegis also asserted Unclean Hands and Patent Misuse. A copy of Aegis' Answer and Counterclaim, as amended, is attached hereto (without exhibits) as Exhibit C.

As is evidenced by the initial pleadings, Ameritox and Aegis are competitors that provide drug testing services. Specifically, Ameritox offers a service called "RxGuardian," pursuant to which it claims it can monitor compliance with pain medicine prescription protocols through the application of an exclusively licensed, proprietary methodology that utilizes patient specific data. Ameritox's testing and compliance monitoring methodology are the subject matter of the Ameritox Patents.

Aegis offers a service called "PainComp," which is offered as a means to determine whether a patient is taking his or her prescribed medication. However, Aegis does not purport to determine whether the patient is taking the proper dosage based on patient specific data. Accordingly, Aegis asserted that it is not violating the Ameritox Patents. Moreover, Aegis has asserted in the Florida Litigation that Ameritox's methodologies are junk science and unpatentable.

As the basis for its unclean hands, unfair competition, patent misuse and sham litigation defenses and counterclaims, Aegis has asserted that Ameritox has "engaged in a concerted effort to disparage and harm the reputation of Aegis" in order to "gain an unfair, improper, and unlawful advantage in its competition with Aegis in the marketplace . . ." Aegis Counterclaim, ¶ 9. Further, Aegis asserts that Ameritox initiated and maintained the Florida litigation as "sham litigation" without regard to the merits of the claims in order to exploit the legal process to the detriment of Aegis "as an anticompetitive weapon." *Id.* *See also*, ¶¶ 36-39 (Sherman Act § 2 Claim).

With respect to the patent misuse claim, Aegis asserted that Ameritox commenced "litigation against Aegis without undertaking the necessary objective prefiling investigation to determine whether the accused products or services infringed the claims of the Patents in suit and

then continuing this litigation knowing that Aegis did not infringe the claims of the Patents in suit." Aegis Counterclaim, ¶ 42.

2. The Attempted Second Amendment Of Ameritox's Complaint And Ameritox's Acknowledgement That Its Patent Claims Are Without Merit.

By motion filed May 8, 2008, Ameritox sought to amend its complaint again. As part of that motion Ameritox sought to dismiss its patent infringement claims "without prejudice" based on its claim that it learned well after it commenced the Florida Litigation that Aegis was not infringing on the Ameritox Patents. A copy of the May 8, 2008 Plaintiffs' Motion for Leave to File Second Amended Complaint is attached hereto as Exhibit D. In order to keep the Florida Litigation alive, Ameritox sought to add a claim for false advertising under the Lanham Act, alleging essentially that Aegis misleads customers into thinking that it provides a service that is similar to Ameritox's service. Aegis disputes this assertion and even asserts that it would never do so because Ameritox's testing methodology is junk science.

Ameritox also filed a Motion to Dismiss the Patent Misuse and Sham Litigation Claims, a copy of which along with the Reply in Support of Motion to Dismiss is attached (without exhibits) hereto as Collective Exhibit E. As part of that argument, Ameritox (and counsel representing Sterling Partners in this action) asserted that to establish a Sherman Act § 2 claim the following factors are relevant:

> -Whether Ameritox (1) engaged in predatory or anti-competitive conduct (2) with the specific intent to monopolize, and (3) a dangerous possibility exists that Plaintiffs will achieve monopoly power. Reply in Support of Motion to Dismiss, p. 2 (citations omitted).
>
> -Whether (1) the lawsuit is objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits; and (2) the party bringing the allegedly baseless lawsuit did so with a subjective motivation to interfere directly with the business relationships of a competitor. Reply In Support of Motion to Dismiss, p. 2 (citations omitted).

> Whether the sham litigation is part of an "anti competitive plan." Reply In Support of Motion to Dismiss, p. 7 (citations omitted).

Likewise, Aegis asserted with respect to its patent misuse affirmative defense that any attempt to broaden the scope of a patent through litigation against a non-infringing competitor, which has an anti competitive effect is patent misuse. Aegis Reply Brief (copy attached as Exhibit E), p. 10 (citations omitted).

By its Order dated July 9, 2008, the Court in the Florida Litigation heard Ameritox's Motion for Leave to File its Second Amended Complaint and its Motion to Dismiss the Patent Misuse and Sham Litigation Claims. A copy of the July 9, 2008 Order is attached hereto as Exhibit F. In that Order the Court characterized Ameritox's Motion to Amend as an attempt to convert its "non viable patent claim into a Lanham act claim by contending that [it] was misled by Defendant's advertisement to believe Plaintiffs' patent was infringed." July 9, 2009 Order, p. 4.

The Florida Court denied Ameritox's attempt to dismiss the sham litigation claim under the Sherman Act § 2 and allowed Aegis to maintain the patent misuse claim as an affirmative defense.

B. Sterling Partners' Relationship With Ameritox

According to Sterling Partners' web site, www.sterlingpartners.com, Sterling Partners is a private equity firm and Ameritox is one of Sterling Partner's portfolio companies. In fact, Sterling Partners states, "We collaborate closely with our management partners to stimulate and sustain significant growth." http://www.sterlingpartners.com/portfolio/index.asp.

Based on Sterling Partners' close relationship with Ameritox, it appears reasonably likely that Ameritox would have discussed with Sterling Partners the viability of this litigation on an objective and subjective basis; the competitive threat of Aegis; Ameritox's actual and/or potential market power within the applicable geographic and product market for its services;

Ameritox's plans to compete (either fairly or unfairly) with Aegis and/or other competitors; and Ameritox's success in the relevant product and geographic market as evidenced by financial data gathered by Sterling Partners.

It is further worth noting that Ameritox and Aegis have a protective order (the "Protective Order") in place in the Florida Litigation, which was approved by Bell, Boyd & Lloyd, so Sterling Partners should have no concerns regarding any confidentiality issues. A copy of the Protective Order entered in the Florida Litigation is attached hereto as Exhibit G.

III. LEGAL ANALYSIS

The burden of persuasion in a motion to quash a subpoena and for a protective order is borne by the movant. *Jones v. Hirschfeld*, 219 F.R.D. 71 (S.D.N.Y. 2003); *Williams v. City of Dallas*, 178 F.R.D. 103, 109 (N.D. Tex. 1998)(movant has burden of proof, and must meet "heavy burden" of establishing that compliance would be unreasonable and oppressive); *Composition Roofers Union Local 30 Welfare Trust Fund v. Graveley Roofing Enters.*, 160 F.R.D. 70, 72 (E.D. Pa. 1995)(court may quash or modify subpoena if movant meets "heavy burden" of establishing that compliance would be unreasonable and oppressive). As is set forth below, Sterling Partners fails to meet its heavy burden of proof because its objections are largely based on blanket assertions and are otherwise hyper technical meritless objections.

A. Sterling Partners' Alleged Claim That Sterling Subpoena Was Improperly Issued Is Without Merit.

Sterling Partners asserts that the subpoena was improperly issued because it cannot tell who signed the Sterling Subpoena. This argument is without merit because (a) John D. Burke, a member of the local bar in good standing with this Court signed the Sterling Subpoena and (b) Sterling Partners knew that John D. Burke signed the Sterling Subpoena because the subpoena directed Sterling Partners to produce the documents at Mr. Burke's offices. Sterling Partners even acknowledges this last fact in footnote 1 of its Motion to Quash.

Moreover, even if no one had signed the Sterling Subpoena, it would remain valid. The failure of an attorney to sign the subpoena is not so substantial a deficiency as to render a subpoena void. *Atlantic Inv. Mgmt. L..C. v. Millennium Fund I, Ltd.*, 212 F.R.D. 395, 397 (N.D. Ill. 2002)(attorney's signature on declaration of service to subpoena evidenced attorney's intent to take responsibility for issuing subpoena). Thus, Sterling Partners' objection to the Sterling Subpoena as being improperly issued, and its feigned inability to tell who issued the subpoena is completely without merit and indicative of the lack of merit of its other objections.

B. The Sterling Subpoena Does Not Improperly Demand Production Of Any Highly Confidential Information.

As its next objection, Sterling Partners asserts that the Sterling Subpoena seeks "highly confidential information." This argument fails for two reasons, and is as disingenuous as the first objection.

First, there is a Protective Order in place in the Florida Litigation that specifically contemplates that third parties may be asked to produce confidential information by providing that it can apply to third parties. Sterling Partners knows about this Protective Order because, by no coincidence, its attorneys are the same attorneys that are representing Ameritox in the Florida Litigation. Yet it fails to mention this to this Court.

Second, Ameritox merely makes a general assertion that certain of the requests (Requests 4, 7, 14 and 17) "encompass all manner of highly confidential documents." However, such general assertions are insufficient. *See Transcor Inv. v. Furney Charters, Inc.*, 212 F.R.D. 588, 592 (D. Kan. 2003)(A general assertion that production would put the responding party "at a competitive disadvantage" was insufficient to meet the "clearly defined and serious injury" standard.)

Given the fact that Sterling Partners' own attorneys have agreed to a Protective Order in the underlying Florida Litigation that protects information that a producing party designates as

CONFIDENTIAL, or HIGHLY CONFIDENTIAL (and thereby restricted to review by outside counsel as opposed to review by the parties), Sterling Partners can hardly object to the production of documents on the basis of confidentiality, particularly when it provides no underlying factual basis for such assertions. Accordingly, this objection is without merit.

C. Sterling Partners' Objections Based On Undue Burden Are Also Without Merit.

Sterling Partners also makes blanket assertions of lack of relevance, undue burden, and attorney client privilege. All of these assertions are without merit.

1. Sterling Partners' Blanket Assertions Of "Undue Burden" Are Insufficient.

A mere statement by a party that a request is "overly broad and unduly burdensome" is not adequate to voice a successful objection. *St. Paul Reinsurance Co. v. Commercial Financial Corp.*, 198 F.R.D. 508, 511-12 (N.D. Ia. 2000). Broad-based, non-specific objections are almost impossible to assess on their merits, and fall woefully short of the burden that must be borne by a party making an objection to an interrogatory or document request. *Harding v. Dana Transport Inc.*, 914 F. Supp. 1084, 1102 (D. N.J. 1996). "A party asserting undue burden typically must present an affidavit or other evidentiary proof of the time or expense involved in responding to the discovery request." *Waddell & Reed Financial, Inc. v. Torchmark Corp.*, 222 F.R.D. 450, 454 (D. Kan. 2004); see also *U.S. ex rel. Fisher v. Network Software Associates*, 217 F.R.D. 240, 246 (D.D.C. 2003); *Wagner v. Dryvit Sys., Inc.*, 208 F.R.D. 606, 610 (D. Neb. 2001); *St. Paul Reinsurance Co., Ltd. v. Commercial Fin. Corp.*, 198 F.R.D. 508, 513 (N.D. Iowa 2000). A party asserting undue burden as a basis for a motion to quash fails to meet its burden when it does not specify the time or resources necessary to comply with subpoena or indicate how compliance would actually be burdensome. *Plant Genetic Sys. N.V. v. Northrup King Co.*, 6 F. Supp. 2d 859, 861 (E.D. Mo. 1998).

To support its undue burden argument, Sterling Partners makes the additional unsupported assertion that documents are available from Ameritox. However, "nothing in the Federal Rules of Civil Procedure requires a litigant to rely solely on discovery obtained from an adversary instead of utilizing subpoenas." *State Farm Mut. Auto. Ins. Co. v. Accurate Medical, P.C.* 2007 WL 2993840 (E.D.N.Y. 2007); *See Covey Oil Co. v. Continental Oil Co.*, 340 F.2d 993, 998 (10th Cir. 1965)("[A] person may not avoid a subpoena by saying that the evidence sought from him is obtainable from another.").

Aegis has legitimate reasons for seeking documents from Sterling Partners. Sterling Partners is the primary, if not the sole, financial investor in Ameritox. It will have performed its own investigations into the market, and it will have been privy to communications with Ameritox that are directly relevant to this case. It is more than likely that it has retained documents that have been lost, misplaced or destroyed by Ameritox and that it has generated documents memorializing and/or relating to communications with Ameritox or information obtained from Ameritox in addition to information relating to competitors and the marketplace.

Thus, Sterling Partners fails to make any showing of undue burden, particularly in light of the relevancy of the requests.

2. Sterling Partners' Blanket Assertions Of Attorney-Client Privilege Are Also Insufficient.

Blanket assertions of the attorney client privilege and/or attorney work product do not warrant quashing a subpoena. *Williams v. City of Dallas*, 178 F.R.D. 103, 109-110 (N.D. Tex. 1998); *Ferko v. NASCAR*, 219 F.R.D. 396, 401-402 (E.D. Tex. 2003)(though work product is protected, party made mere blanket assertion that materials sought by subpoena were work product, so motion to quash denied). A court will deny the motion to quash when the objections fail to show how the requests "specifically invade" the privilege. *Stock*, 241 F.R.D. at 622. A motion to quash is properly denied where the party resisting disclosure fails to produce a

document index or privilege log sufficient to support the propriety of the claim. *In re Grand Jury Subpoena*, 274 F.3d 563, 575-576 (3d Cir. 2001).

The instructions contained in the subpoena provide the accepted mechanism for providing a log of any documents that Sterling Partners asserts are privileged so that Aegis can make a determination of whether the assertions have merit. Sterling Subpoena, Instruction No. 1. A blanket assertion does not allow either Aegis or this Court to determine whether such assertions have merit.

3. The Requests Are Clearly Relevant And Reasonably Calculated To Lead To the Production Of Relevant Evidence.

With respect to relevancy, Courts adopt the standard of Fed. R. Civ. P. 26, whether the requests are "reasonably calculated to lead to the discovery of admissible evidence." *See Stock v. Integrated Health Plan*, 241 F.R.D. 618, 621 (S.D. Ill. 2007).

With respect to the requests, Aegis states as follows:

1. All documents referring to or evidencing any communications between Ameritox and Sterling Partners referring to Aegis and/or PainComp.

Relevance: It is reasonably, if not highly, likely that Ameritox has had communications with Sterling Partners about Aegis with Ameritox, including its plan for competing (fairly or unfairly) with Aegis and any determination as to whether it actually believes that Aegis was infringing on its patent or causing it harm in the marketplace. It is also reasonably likely that Sterling Partners may have generated its own internal documents assessing such communications.

2. All documents referring to or evidencing any communications between Ameritox and Sterling Partners referring to any other entities (including Aegis) that compete with Ameritox with respect to RxGuardian.

Relevance: It is reasonably, if not highly, likely that Ameritox has had communications with Sterling Partners about other competitors, which is relevant to whether Ameritox's conduct as it relates to Aegis is part of a more wide spread effort to thwart competition, which would be relevant to the unclean hands and sham litigation claim insofar as it would evidence subjective bad faith and an attempt to monopolize.

3. All documents referring to or evidencing any communications between Ameritox and Sterling Partners referring to this Lawsuit, the bringing of this Lawsuit, the

allegations in the Lawsuit, and/or any dispute between Ameritox and Aegis, including, but not limited to, any other lawsuits between the parties.

Relevance: It is reasonably, if not highly, likely that Ameritox has had communications with Sterling Partners about the Florida Lawsuit, particularly since they are represented by the same legal counsel. These communications may evidence Ameritox's objective and subjective intent with respect to the Florida Lawsuit, including Ameritox's and/or Sterling Partner's knowledge regarding whether Aegis was actually infringing on Ameritox's patent, and whether Ameritox had ulterior motives for bringing the Florida Lawsuit that were shared with or considered by Sterling Partners.

4. All documents referring to or evidencing any internal communications, discussions or considerations regarding and/or relating to (a) the financial performance of Ameritox; (b) the financial performance of RxGuardian; (c) the Lawsuit; (d) Aegis; (e) PainComp; (f) the market for RxGuardian; (d) the market (product and/or geographic) for services or products that compete with RxGuardian; and (e) market share held by RxGuardian.

Relevance: The documents sought in this request are directly relevant to whether Ameritox is attempting to monopolize, whether it has monopoly power, and whether it has been successful in acquiring market share and financial performance. It is highly likely that Ameritox would have provided its financial investor with information in this regard, and that Sterling Partners, as the financial investor of Ameritox, would have generated its own analysis of market and financial data relating to Ameritox. Ameritox's representations as to its market share and its desire to increase its market share are relevant to the sham litigation claim.

5. All documents relating to or evidencing the marketing, and/or sales of RxGuardian, including but not limited to any pro forma projection(s), marketing brochures, actual sales/leasing information, advertisements (in final and draft form), and marketing proposals.

Relevance: See response to Request No. 4.

6. All documents relating to or evidencing any studies or research relating to the actual or potential product and/or geographic market for RxGuardian or similar products and/or services.

Relevance: See response to Request No. 4.

7. All documents, including drafts, prepared by for or on behalf of Ameritox and/or Sterling Partners for the purpose of obtaining loans or financing for and/or equity investment in Ameritox, including, but not limited to any prospectuses, private placement memoranda, pro formas or any similar documents.

Relevance: See response to Request No. 4. It is reasonably likely that Ameritox has sought other investors and that Sterling Partners has assisted Ameritox in seeking additional investment (either equity or debt), and in that regard, Sterling Partners and/or

Ameritox have generated documents that address market share, market power and market and financial success of Ameritox.

8. All documents that describe, discuss and/or refer to the market for RxGuardian, including the product and/or geographic market for RxGuardian.

Relevance: See response to Request No. 4.

9. All documents that describe, discuss and/or refer to market share held by Ameritox and/or RxGuardian.

Relevance: See response to Request No. 4.

10. All documents that support or relate to the assertion by Ameritox on its website that it is the "nation's leader in pain prescription monitoring."

Relevance: Sterling Partners does not dispute that Ameritox makes this assertion on its web site. This assertion supports Aegis's assertion that Ameritox has market power and is relevant to whether Ameritox filed the Florida Lawsuit to increase and/or protect its market power. As the financial investor in Ameritox, it is highly likely that Sterling Partners has documents that it either generated internally or obtained from Ameritox that discuss or relate to competitors in the pain prescription monitoring business and Ameritox's position in that business.

11. All documents that evaluate, refer to, and/or discuss (a) the market for pain prescription monitoring; (b) the customer base for pain prescription monitoring; and (c) competition in the pain prescription monitoring business.

Relevance: See response to Request Nos. 4 and 10.

12. All documents relating to or evidencing any attempts to induce or persuade Aegis and/or PainComp customers to use RxGuardian or to not use Aegis and/or PainComp.

Relevance: This request is directly relevant to whether Ameritox is attempting to unfairly compete with Aegis and disparage Aegis. As the financial investor in Ameritox, it is highly likely that Sterling Partners may have generated documents or obtained documents from Ameritox that are responsive to this request.

13. All documents relating to or evidencing any direct or indirect communications to any actual or potential customer for RxGuardian or PainComp that references, mentions or discusses Aegis, PainComp, the Lawsuit or any issues raised in the Lawsuit.

Relevance: See response to Request No. 12.

14. All documents relating to the finances and/or financial performance of Ameritox, including but not limited to budgets, pro-forma financial statements, actual financial statements, reports, and memoranda.

Relevance: See response to Request Nos. 4 and 10.

15. All correspondence or any other documents evidencing or relating to any communications with any other entities, including actual or potential customers of Aegis or Ameritox, regarding or relating to Aegis or any goods and services provided by Aegis, including but not limited to PainComp.

Relevance: See response to Request No. 12. These documents are also relevant to Ameritox's subjective intent with respect to filing the Florida Lawsuit.

16. All correspondence or any other documents evidencing or relating to any communications with any other entities, regarding or relating to any other providers of products and/or services that compete with PainComp and/or RxGuardian.

Relevance: See response to Request Nos. 12 and 15.

17. All documents, not already produced, relating to or evidencing any market studies performed in connection with the development RxGuardian from the beginning of its development to the present. (This request extends beyond the operative time period set forth in the instructions).

Relevance: See response to Request No. 4.

18. All documents, not already produced, that in any way compare, contrast or otherwise distinguish RxGuardian from any competitor.

Relevance: See response to Request No 4.

19. All documents that refer to, discuss or evidence any disputes, controversies or lawsuits between Ameritox and any other competitor of Ameritox or any other company engaged in the pain prescription monitoring business.

Relevance: The document sought in this request are relevant to Ameritox's subjective intent in bringing the Florida Litigation and whether the Florida Litigation is part of a larger effort by Ameritox to protect or enhance its market power. As Ameritox's primary investor, it is reasonably likely that Sterling Partners may have generated or obtained documents responsive to this request.

Based on the foregoing, it is clear that Aegis's requests are relevant insofar as they are "reasonably calculated to lead to the discovery of admissible evidence," that they are not unduly

burdensome. Therefore, Sterling Partners' arguments (which are being asserted by counsel for Ameritox) are without merit.

IV. CONCLUSION

FOR THE FOREGOING REASONS, the Motion to Quash should be denied.

AEGIS SCIENCES, CORP.

By: /s/ John D. Burke
One of Its Attorneys

John D. Burke (ARDC No. 06203918)
ICE MILLER, LLP
200 West Madison, Suite 3500
Chicago, Illinois 60606
(312) 726-5147

CERTIFICATE OF SERVICE

John D. Burke, an attorney, certifies that on August 22, 2008, he served a copy of **Defendant's Response in Opposition to Motion to Quash** by electronic mail and U.S. Mail, proper postage prepaid, upon:

Michael R. Osterhoff, Esq.
Bell, Boyd & Lloyd, LLP
70 West Madison, Suite 3100
Chicago, Illinois 60606-4207

/s/ John D. Burke
John D. Burke

EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS

AMERITOX, LTD. and U.D. TESTING, INC.	)	
	)	
Plaintiffs,	)	
v.	)	NO. 07 C 80498
	)	
AEGIS SCIENCES CORP.,	)	
	)	
Defendant.	)	

NOTICE OF SUBPOENA

To: See attached Certificate of Service.

PLEASE TAKE NOTICE that pursuant to the applicable rules of the Federal Code of Civil Procedure and the local rules for this district, we served the attached subpoena upon Sterling Partners, c/o Tom D. Wippman, 1033 Skokie Blvd., Suite 600, Northbrook, Illinois 60062, by special process server.

Dated: July 25, 2008

AEGIS SCIENCES CORP.

BY: _____
One of Its Attorneys

John D. Burke
ICE MILLER LLP/18065
200 West Madison, Suite 3500
Chicago, Illinois 60606
(312) 726-7145

CERTIFICATE OF SERVICE

John D. Burke, an attorney, certifies that on July 25, 2008, he served a copy of **Defendant's Notice of Subpoena** by U.S. Mail, proper postage prepaid, upon:

James A. Gale, Esq.
Christopher P. Demetriades, Esq.
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John D. Burke

C/68542.1

AO88 (Rev. 12/07) Subpoena in a Civil Case

Issued by the

UNITED STATES DISTRICT COURT

Northern District of Illinois

AMERITOX, LTD.and U.D. TESTING, INC.

V.

AEGIS SCIENCES CORP.

SUBPOENA IN A CIVIL CASE
DUCES TECUM

Case Number:[1] 07-80498
Case Presently Pending in the U.S. District Court for the Southern District of Florida

TO: Sterling Partners
c/o Tom D. Wippman
1033 Skokie Blvd., Suite 600
Northbrook, Illinois 60062

☐ YOU ARE COMMANDED to appear in the United States District court at the place, date, and time specified below to testify in the above case.

PLACE OF TESTIMONY	COURTROOM
	DATE AND TIME

☐ YOU ARE COMMANDED to appear at the place, date, and time specified below to testify at the taking of a deposition in the above case.

PLACE OF DEPOSITION [TO BE PROVIDED]	DATE AND TIME

☑ YOU ARE COMMANDED to produce and permit inspection and copying of the following documents or objects at the place, date, and time specified below (list documents or objects):

SEE ATTACHED EXHIBIT "A"

PLACE	DATE AND TIME
John D. Burke/Ice Miller LLP 200 W. Madison, Suite 3500, Chicago, IL 60606	8/14/2008 11:00 am

☐ YOU ARE COMMANDED to permit inspection of the following premises at the date and time specified below.

PREMISES	DATE AND TIME

Any organization not a party to this suit that is subpoenaed for the taking of a deposition shall designate one or more officers, directors, or managing agents, or other persons who consent to testify on its behalf, and may set forth, for each person designated, the matters on which the person will testify. Federal Rule of Civil Procedure 30(b)(6).

ISSUING OFFICER'S SIGNATURE AND TITLE (INDICATE IF ATTORNEY FOR PLAINTIFF OR DEFENDANT)	DATE
Defendant	7/25/2008

ISSUING OFFICER'S NAME, ADDRESS AND PHONE NUMBER

(See Federal Rule of Civil Procedure 45 (c), (d), and (e), on next page)

[1] If action is pending in district other than district of issuance, state district under case number.

PROOF OF SERVICE

DATE PLACE

SERVED

SERVED ON (PRINT NAME) MANNER OF SERVICE

SERVED BY (PRINT NAME) TITLE

DECLARATION OF SERVER

I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in the Proof of Service is true and correct.

Executed on _____
DATE

SIGNATURE OF SERVER

ADDRESS OF SERVER

Federal Rule of Civil Procedure 45 (c), (d), and (e), as amended on December 1, 2007:

(c) PROTECTING A PERSON SUBJECT TO A SUBPOENA.

(1) Avoiding Undue Burden or Expense; Sanctions. A party or attorney responsible for issuing and serving a subpoena must take reasonable steps to avoid imposing undue burden or expense on a person subject to the subpoena. The issuing court must enforce this duty and impose an appropriate sanction — which may include lost earnings and reasonable attorney's fees — on a party or attorney who fails to comply.

(2) Command to Produce Materials or Permit Inspection.

(A) Appearance Not Required. A person commanded to produce documents, electronically stored information, or tangible things, or to permit the inspection of premises, need not appear in person at the place of production or inspection unless also commanded to appear for a deposition, hearing, or trial.

(B) Objections. A person commanded to produce documents or tangible things or to permit inspection may serve on the party or attorney designated in the subpoena a written objection to inspecting, copying, testing or sampling any or all of the materials or to inspecting the premises — or to producing electronically stored information in the form or forms requested. The objection must be served before the earlier of the time specified for compliance or 14 days after the subpoena is served. If an objection is made, the following rules apply:

(i) At any time, on notice to the commanded person, the serving party may move the issuing court for an order compelling production or inspection.

(ii) These acts may be required only as directed in the order, and the order must protect a person who is neither a party nor a party's officer from significant expense resulting from compliance.

(3) Quashing or Modifying a Subpoena.

(A) When Required. On timely motion, the issuing court must quash or modify a subpoena that:

(i) fails to allow a reasonable time to comply;

(ii) requires a person who is neither a party nor a party's officer to travel more than 100 miles from where that person resides, is employed, or regularly transacts business in person — except that, subject to Rule 45(c)(3)(B)(iii), the person may be commanded to attend a trial by traveling from any such place within the state where the trial is held;

(iii) requires disclosure of privileged or other protected matter, if no exception or waiver applies; or

(iv) subjects a person to undue burden.

(B) When Permitted. To protect a person subject to or affected by a subpoena, the issuing court may, on motion, quash or modify the subpoena if it requires:

(i) disclosing a trade secret or other confidential research, development, or commercial information;

(ii) disclosing an unretained expert's opinion or information that does not describe specific occurrences in dispute and results from the expert's study that was not requested by a party; or

(iii) a person who is neither a party nor a party's officer to incur substantial expense to travel more than 100 miles to attend trial

(C) Specifying Conditions as an Alternative. In the circumstances described in Rule 45(c)(3)(B), the court may, instead of quashing or modifying a subpoena, order appearance or production under specified conditions if the serving party:

(i) shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship; and

(ii) ensures that the subpoenaed person will be reasonably compensated.

(d) DUTIES IN RESPONDING TO A SUBPOENA.

(1) Producing Documents or Electronically Stored Information. These procedures apply to producing documents or electronically stored information:

(A) Documents. A person responding to a subpoena to produce documents must produce them as they are kept in the ordinary course of business or must organize and label them to correspond to the categories in the demand.

(B) Form for Producing Electronically Stored Information Not Specified. If a subpoena does not specify a form for producing electronically stored information, the person responding must produce it in a form or forms in which it is ordinarily maintained or in a reasonably usable form or forms.

(C) Electronically Stored Information Produced in Only One Form. The person responding need not produce the same electronically stored information in more than one form.

(D) Inaccessible Electronically Stored Information. The person responding need not provide discovery of electronically stored information from sources that the person identifies as not reasonably accessible because of undue burden or cost. On motion to compel discovery or for a protective order, the person responding must show that the information is not reasonably accessible because of undue burden or cost. If that showing is made, the court may nonetheless order discovery from such sources if the requesting party shows good cause, considering the limitations of Rule 26(b)(2)(C). The court may specify conditions for the discovery.

(2) Claiming Privilege or Protection.

(A) Information Withheld. A person withholding subpoenaed information under a claim that it is privileged or subject to protection as trial-preparation material must:

(i) expressly make the claim; and

(ii) describe the nature of the withheld documents, communications, or tangible things in a manner that, without revealing information itself privileged or protected, will enable the parties to assess the claim.

(B) Information Produced. If information produced in response to a subpoena is subject to a claim of privilege or of protection as trial-preparation material, the person making the claim may notify any party that received the information of the claim and the basis for it. After being notified, a party must promptly return, sequester, or destroy the specified information and any copies it has; must not use or disclose the information until the claim is resolved; must take reasonable steps to retrieve the information if the party disclosed it before being notified; and may promptly present the information to the court under seal for a determination of the claim. The person who produced the information must preserve the information until the claim is resolved.

(e) CONTEMPT.

The issuing court may hold in contempt a person who, having been served, fails without adequate excuse to obey the subpoena. A nonparty's failure to obey must be excused if the subpoena purports to require the nonparty to attend or produce at a place outside the limits of Rule 45(c)(3)(A)(ii).

EXHIBIT "A"

DEFINITIONS

1. The term "Ameritox" refers to Ameritox, Ltd. its subsidiaries, affiliates, merged, consolidated or acquired predecessors, divisions, and holding or parent companies, at any time relevant hereto, its agents, including attorneys, accountants, employees, and anyone else acting or purporting to act on its behalf.

2. The term "RxGuardian" refers to Ameritox's product/services and/or bundle of products and/or services offered under that trade name.

3. The term "PainComp" refers to that product/service and/or bundle of products and/or services offered by Aegis Analytical Labs, Inc. ("Aegis").

4. The term "referring" means concerning, disclosing, embodying, relating, or referring to, directly or indirectly in any manner.

5. The term "Sterling Partners" refers to Sterling Partners including, without limitation, its subsidiaries, affiliates, merged, consolidated or acquired predecessors, divisions, holding or parent companies, and partners, and any funds owned or controlled by Sterling Partners at any time relevant hereto, its agents, including accountants, attorneys, employees, and anyone else acting or purporting to act on its behalf.

6. The term "documents" means writings or electronically stored information of any kind (whether printed, typed, photocopied, handwritten, recorded, stored, or produced or reproduced by any other process), or any other compilation of information that is in the possession, custody or control of you or your attorneys or agents, and is used in the broadest sense permissible under Rule 34 of the Federal Rules of Civil Procedure and includes, without limitation, any and all:

a. accountants and other worksheets, advertisements, advertising circulars, advisories, agreements, appointment books, articles, books, brochures, bulletins, calendars, charts, checks, communications (intra-office, interoffice, external and other), computer printouts, contracts, correspondence, desk-pads, diaries, drafts, drawings, flyers, forecasts, graphs, guidelines, instructions, invoices, letters, lists, logs, memoranda, minutes of meetings, newspaper clippings, notebooks, notes, periodicals, post-it notes, projections, receipts, records, reports, rules, statements, studies, summaries, telecopies, telegrams, telephone messages, telexes, transcripts and translations;

b. graphic or audio records or representations of any kind (including, but not limited to, photography, charts, drawings, graphs, microfiche, microfilm, videotapes, recordings and motion pictures);

c. electric, electronic, magnetic, mechanical and optical records or representations of any kind (including, but not limited to tapes, cassettes, disks, recordings, computer memories, emails and electronically stored information); and

d. drafts and final versions, and all originals as well as copies that differ from originals in any respect (including, but not limited to, differences due to handwritten notes, editing, interlineations, blind copies or any other alterations).

7. The term "communication" means every disclosure or exchange of information, whether written, face-to-face, telephonic, personal delivery or any other form of communicating information.

8. The terms "all" and "each" shall be construed as "all and each."

9. The connectives "and" and "or" shall be construed disjunctively or conjunctively as necessary to bring within the scope of these Requests all responses that might otherwise be construed as outside of their scope.

10. The use of the singular form of any word includes the plural and vice-versa.

11. "Lawsuit" shall refer to the lawsuit captioned in this subpoena.

INSTRUCTIONS

1. To the extent any Request is objected to, set forth all reasons for making the objection. If you object to only a part of a Request, respond to the remainder of the Request. With respect to any document for which you claim a privilege, identify the document, including (a) the privilege involved, and (b) the general subject matter (but not the substance) of the document in sufficient detail so as to permit the Court to adjudicate the validity of your objections.

2. For the purposes of this subpoena, unless otherwise stated below, the operative time period for the documents requested herein is from January 1, 2003 to the present unless otherwise stated below.

REQUESTS

1. All documents referring to or evidencing any communications between Ameritox and Sterling Partners referring to Aegis and/or PainComp.

2. All documents referring to or evidencing any communications between Ameritox and Sterling Partners referring to any other entities (including Aegis) that compete with Ameritox with respect to RxGuardian.

3. All documents referring to or evidencing any communications between Ameritox and Sterling Partners referring to this Lawsuit, the bringing of this Lawsuit, the allegations in the Lawsuit, and/or any dispute between Ameritox and Aegis, including, but not limited to, any other lawsuits between the parties.

4. All documents referring to or evidencing any internal communications, discussions or considerations regarding and/or relating to (a) the financial performance of Ameritox; (b) the financial performance of RxGuardian; (c) the Lawsuit; (d) Aegis; (e) PainComp; (f) the market for RxGuardian; (d) the market (product and/or geographic) for services or products that compete with RxGuardian; and (e) market share held by RxGuardian.

5. All documents relating to or evidencing the marketing, and/or sales of RxGuardian, including but not limited to any pro forma projection(s), marketing brochures, actual sales/leasing information, advertisements (in final and draft form), and marketing proposals.

6. All documents relating to or evidencing any studies or research relating to the actual or potential product and/or geographic market for RxGuardian or similar products and/or services.

7. All documents, including drafts, prepared by for or on behalf of Ameritox and/or Sterling Partners for the purpose of obtaining loans or financing for and/or equity investment in Ameritox, including, but not limited to any prospectuses, private placement memoranda, pro formas or any similar documents.

8. All documents that describe, discuss and/or refer to the market for RxGuardian, including the product and/or geographic market for RxGuardian.

9. All documents that describe, discuss and/or refer to market share held by Ameritox and/or RxGuardian.

10. All documents that support or relate to the assertion by Ameritox on its website that it is the "nation's leader in pain prescription monitoring."

11. All documents that evaluate, refer to, and/or discuss (a) the market for pain prescription monitoring; (b) the customer base for pain prescription monitoring; and (c) competition in the pain prescription monitoring business.

12. All documents relating to or evidencing any attempts to induce or persuade Aegis and/or PainComp customers to use RxGuardian or to not use Aegis and/or PainComp.

13. All documents relating to or evidencing any direct or indirect communications to any actual or potential customer for RxGuardian or PainComp that references, mentions or discusses Aegis, PainComp, the Lawsuit or any issues raised in the Lawsuit.

14. All documents relating to the finances and/or financial performance of Ameritox, including but not limited to budgets, pro-forma financial statements, actual financial statements, reports, and memoranda.

15. All correspondence or any other documents evidencing or relating to any communications with any other entities, including actual or potential customers of Aegis or Ameritox, regarding or relating to Aegis or any goods and services provided by Aegis, including but not limited to PainComp.

16. All correspondence or any other documents evidencing or relating to any communications with any other entities, regarding or relating to any other providers of products and/or services that compete with PainComp and/or RxGuardian.

17. All documents, not already produced, relating to or evidencing any market studies performed in connection with the development RxGuardian from the beginning of its development to the present. (This request extends beyond the operative time period set forth in the instructions).

18. All documents, not already produced, that in any way compare, contrast or otherwise distinguish RxGuardian from any competitor.

19. All documents that refer to, discuss or evidence any disputes, controversies or lawsuits between Ameritox and any other competitor of Ameritox or any other company engaged in the pain prescription monitoring business.

EXHIBIT B

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA
WEST PALM BEACH DIVISION

AMERITOX, LTD., and U.D. TESTING, INC.,	)	
Plaintiffs,	)	
	)	Civil Action No.
v.	)	
	)	Jury Trial Demanded
AEGIS SCIENCES CORP.,	)	Injunctive Relief Sought
Defendant.	)	

FIRST AMENDED COMPLAINT

Plaintiffs Ameritox Limited ("Ameritox") and U.D. Testing, Inc. (UDT) (collectively "Plaintiffs") for its complaint against defendant Aegis Sciences Corporation ("Aegis"), seeking damages, injunctive relief and other relief for patent infringement, tortious interference, deceptive practices, and false marking allege as follows:

PARTIES, JURISDICTION AND VENUE

1. Ameritox is a Texas limited partnership with its principal place of business at 3510 North A Street, Building B, Suite 200, Midland, Texas 79705.

2. UDT is a Florida corporation with its principle place of business at 950 North Collier Boulevard, Suite 207, Marco Island, Florida 34145.

3. Upon information and belief, Defendant Aegis is a Tennessee corporation with its principal place of business at 345 Hill Avenue, Nashville, Tennessee 37210 and is offering for sale, selling, and using the infringing methods in the United States and the Southern District of Florida.

4. Aegis makes, uses, sells and offers for sale throughout the United States, including within this judicial district, methods of monitoring patient compliance that infringe

UDT's United States Patent Nos. 5,908,788 and 6,124,136 ("patents in suit"). The patents in suit are attached hereto as Exhibits A and B. Upon information and belief, Aegis has substantial and not isolated contacts with the State of Florida and has committed acts of infringement in the State of Florida, including the Southern District of Florida, sufficient to confer personal jurisdiction upon Aegis.

5. This Court has jurisdiction over Plaintiffs patent infringement claims pursuant to 28 U.S.C. §§ 1331 and 1338(a).

6. Venue properly lies in this Court under 28 U.S.C. §§ 1391(b), (c) and 1400(b) because Aegis is subject to personal jurisdiction and has committed acts of patent infringement in the Southern District of Florida.

FACTUAL BACKGROUND

7. On June 1, 1999, United States Patent No. 5,908,788 ("'788 Patent") was duly and legally issued for an invention entitled "Method of Monitoring Patient Compliance with Medications Prescriptions." A copy of the '788 Patent is attached hereto as Exhibit A. The named inventor of the '788 patent is Michael Kell and the patent was properly assigned to UDT.

8. On September 26, 2000, United States Patent No. 6,124,136 ("'136 Patent") was duly and legally issued for an invention entitled "Method of Monitoring Compliance with Methadone Treatment Program." A copy of the '136 Patent is attached hereto as Exhibit B. The named inventor of the '136 is Michael Kell and the patent was properly assigned to UDT.

9. On or about March 1, 2005, Ameritox became the exclusive licensee of the '788 Patent and the '136 Patent.

RxGUARDIAN PAIN PRESCRIPTION MONITORING

10. Recent studies suggest that a large percentage of chronic pain patients do not comply with their physicians' orders and either take too much of a prescribed medication, not

enough of a prescribed medication, or mix the prescribed medication with other legal and illegal drugs.

11. Ameritox is a national leader in pain prescription monitoring.

12. Ameritox provides pain prescription monitoring services throughout the United States, including the RxGuardian Pain Prescription Monitoring ("RxGuardian") program.

13. Amertiox's RxGuardian is contracted to physicians and clinics.

14. Amertitox's RxGuardian lets physicians monitor their patients' compliance with a prescription drug regimen by comparing normalized urine values to established, prescription-specific ranges. Unlike traditional drug-monitoring services, RxGaurdian uses a patented algorithm to personalize lab results according to patient demographics (height, weight, gender, age) and prescription regimen. In addition, RxGuardian allows the physicians to detect whether their patients are taking any other medications or illegal narcotics that might interfere with the prescribed drug regimen and/or cause a potentially dangerous drug interaction.

15. Amertiox's RxGuardian takes place in several stages. First, urine samples are collected from a physician who indicates what information is desired in the analysis. A urine sample may be provided to Ameritox directly from the physician. Otherwise, a third party collector ("collector") will pick up the urine sample on Ameritox's behalf and deliver it to the laboratory for testing.

16. After receipt of the urine sample, Amertiox runs a battery of tests. The first series of tests determine if any of the drugs that the physician is looking for are present. If the target drug(s) is identified, a second series of tests is run to identify each specific compound in the patient's system. The patented algorithm allows Amertiox to compare the amount of a particular

compound in the patient's system with the prescribed rate. A sample RxGuardian Report is attached hereto as Exhibit C.

17. According to a recent study presented at the 2007 International Conference of Pain and Chemical Dependency, Ameritox's RxGuardian hydrocodone algorithm predicts "with a 95 percent confidence limit" whether patients were taking their hydrocodone pain medication as prescribed.

AEGIS' PATTERN OF UNLAWFUL, DECEPTIVE AND UNFAIR PRACTICES

18. Aegis is a direct competitor of Ameritox in the drug testing industry.

19. Upon information and belief, Aegis makes, uses, sells and offers for sale monitoring methods that infringe the patents in suit.

20. Aegis has engaged in a pattern of unlawful, improper, deceptive and unfair practices in order to harm Amertiox's reputation in the marketplace and to gain an unfair business advantage.

21. Upon information and belief, Aegis is aware of, and calls on, clients of Ameritox. Aegis offers "free" sample cups to Ameritox clients for their use. Aegis will only provide additional "free" sample cups if the Ameritox client uses the services of Aegis instead of those of Ameritox in violation of the Medicare Fraud and Abuse Act.

22. Upon information and belief, Aegis uses the same third party collectors as Ameritox. However, Aegis pays the collectors a higher rate in an effort to have them persuade Ameritox clients, and potential clients, to use the services of Aegis.

23. Upon information and belief, Aegis offers Ameritox clients a cash pay option where any patient of the clinic whose insurance claim is denied for using the Aegis services pays only a flat fee for the service.

24. Aegis also provides reports for its clients. However, the Aegis reports are substantial copies of those created by Ameritox, yet Aegis passes them off as their own.

25. Upon information and believe, Aegis and its agents, employees and/or sales representatives, have also made false and misleading representations to Ameritox in an effort to gain access to the information that Ameritox provides to new clients. In September, 2007, Ameritox opened a new account with Dr. Jonathan M. Greer at the Arthritis and Rheumatology Associates of Palm Beach, which is located at 1600 South Congress Ave., Suite 201, Palm Springs, Florida. On September 17, 2007, Ameritox's agents, Juan Saldarriaga ("Saldarriaga") and Frank Baquedano ("Baquedano"), met with Dr. Greer at his office to train his staff on Ameritox's product. Dr. Greer instructed Ameritox to provide training to his medical assistant, whom he referred to as "Nicole.". Ameritox worked with the medical assistant for several hours, providing her with all of the information that it provides new clients about its product. Ameritox trained her on the collection of samples, completion of Ameritox's forms, and provided information regarding billing and shipping. As part of the training, Ameritox also provided the medical assistant with a clinic binder that contains examples of requisition forms, information regarding Ameritox's products, financial policies, order forms and other information. Through the course of this training, Ameritox worked with the medical assistant to collect eleven urine samples to be tested by Ameritox. After this initial meeting, Dr. Greer's office never submitted another sample for testing.

26. Between November 15 and 17, 2007, Saldarriaga attended the American Society of Regional Anesthesia Pain Management Conference in Boca Raton, Florida. While working at the conference, Mr. Saldarriaga encountered the medical assistant who allegedly worked for Dr. Greer. She was working at the Aegis booth as an Aegis representative.

27. On or about November 28, 2007, Dr. Greer informed Baquedano that he would no longer be using Ameritox's services.

28. Ameritox has been substantially damaged as a result of the unlawful, deceptive, unfair and tortious practices of Aegis.

COUNT I

Patent Infringement of U.S. Patent No. 5,908,788

29. Plaintiffs reallege and incorporate by reference the allegations in Paragraphs 1 through 28 of its Complaint.

30. By making, using, importing, selling, and/or offering to sell their drug monitoring services, Aegis has infringed one or more claims of the '788 Patent directly, contributorily, and/or through inducement. Aegis has engaged in the foregoing conduct with respect to the patented invention in the United States without authority from UDT or Ameritox and during the term of the '788 Patent.

31. Upon information and belief, Aegis will not stop using, selling, and/or offering for sale the methods at issue to avoid infringing the '788 Patent.

32. Upon information and belief, Aegis' infringement has been deliberate, willful and wanton, and with full knowledge of the '788 Patent.

33. Aegis' conduct has caused Plaintiffs to suffer and, unless enjoined by the Court, will cause Plaintiffs to continue to suffer damage to its operation, reputation, and goodwill.

34. Plaintiffs have no adequate remedy at law. Aegis' conduct has caused and, if not enjoined, will continue to cause irreparable damage to Plaintiffs. As a result of Aegis' wrongful conduct, Plaintiffs are entitled to injunctive relief.

COUNT II

Patent Infringement of U.S. Patent No. 6,124,136

35. Plaintiffs reallege and incorporates by reference the allegations in Paragraphs 1 through 34 of its Complaint.

36. By using, selling, and/or offering to sell their drug monitoring services, Aegis has infringed one or more claims of the '136 Patent directly, contributorily, and/or through inducement. Aegis has engaged in the foregoing conduct with respect to the patented invention in the United States without authority from UDT or Ameritox and during the term of the '136 patent.

37. Upon information and belief, Aegis will not stop using, selling, and/or offering for sale the methods at issue to avoid infringing the '136 Patent.

38. Upon information and belief, Aegis' infringement has been deliberate, willful and wanton, and with full knowledge of the '136 Patent.

39. Aegis' conduct has caused Plaintiffs to suffer and, unless enjoined by the Court, will cause Plaintiffs to continue to suffer damage to its operation, reputation, and goodwill.

40. Plaintiffs have no adequate remedy at law. Aegis' conduct has caused and, if not enjoined, will continue to cause irreparable damage to Plaintiffs. As a result of Aegis' wrongful conduct, Plaintiffs are entitled to injunctive relief.

COUNT III

Florida Deceptive and Unfair Trade Practices Act

41. Plaintiff realleges and incorporates by reference the allegations in Paragraphs 1 through 40 of its Complaint.

42. Upon information and belief, Aegis has, and continues to misrepresent the quality and nature of its services and reports. Such misrepresentations are likely to mislead and deceive

customers. Customers that believe Aegis' claims will and have used Aegis' services instead of those of Ameritox.

43. Aegis has also misrepresented itself to Ameritox in an effort to gain information regarding the information it provides to new clients, including the nuances of Ameritox's products.

44. Aegis' conduct constitutes deceptive trade practices under Fl. Ann. Stat. §§ 501.201-213.

45. As a direct and proximate result of Aegis' conduct, Ameritox has incurred actual damages and is entitled to all remedies available under the law.

COUNT IV

Tortious Interference with Business Relationships

46. Plaintiff realleges and incorporates by reference the allegations in Paragraphs 1 through 45 of its Complaint.

47. Ameritox has accounts with numerous client clinics, including those that employ third parties to collect samples from the patients of the client clinics, and is constantly working to establish business relationships with new doctors and clinics.

48. Upon information and belief, Aegis has knowledge of Ameritox client clinics, particularly Ameritox client clinics that employ third parties used to collect samples.

49. Upon information and belief, Aegis intentionally and unjustifiably interfered with the relationships between Ameritox and its clinic accounts. Aegis offered Ameritox client clinics with free sample cups on the condition the client clinic no longer use Ameritox, but use Aegis instead for its drug monitoring services. In addition, Aegis has offered to pay the third party collectors more money in an effort to further persuade Ameritox clients to use the services of Aegis.

50. Aegis has also interfered with Ameritox's business relationships by working with Ameritox's clients and posing as employees of those clinics to gain proprietary information from Ameritox.

51. As a direct and proximate result of Defendant's conduct, Ameritox has been damaged by Aegis' tortious interference with Ameritox's business relationships and is entitled to all remedies available under the law.

COUNT V

Fraudulent Misrepresentation

52. Plaintiffs reallege and incorporates by reference the allegations in Paragraphs 1 through 51 of its Complaint.

53. Upon information and belief, Aegis' agent's representation that she was a medical assistant for Dr. Greer was a misrepresentation of a material fact.

54. Upon information and belief, Aegis knew this fact to be false at the time it made the misrepresentation.

55. Aegis' misrepresentation was made with the intention of inducing Ameritox to rely upon it.

56. Ameritox relied upon the misrepresentation to its detriment.

57. Ameritox's reliance upon Aegis' misrepresentation has caused Ameritox to suffer damages.

58. As a direct and proximate result of Defendant's conduct, Ameritox has been damaged and is entitled to all remedies available under the law.

COUNT VI

False Marking

59. Plaintiffs reallege and incorporate by reference the allegations in Paragraphs 1 through 58 of its Complaint.

60. Aegis, on its web site, advertises that its "Targeted High School Drug Testing Program" included Defendant's "patented Zero-Tolerance Drug Testing..." This program is offered for sale and sold within the United States, including within this District.

61. On August 6, 2007, counsel for Ameritox contacted counsel for Aegis and requested that it identify the patent number under which Aegis advertised its Zero-Tolerance Testing process. A copy of the letter is attached as Exhibit D.

62. On August 8, 2007, counsel for Aegis confirmed that Zero-Tolerance Testing is not a patented product and that Aegis had removed "this error" from its web-site. A copy of the letter is attached as Exhibit E.

63. As of December 21, 2007, Aegis continues to advertise that its "Targeted High School Drug Testing Program" included Defendant's "patented Zero-Tolerance Drug Testing..." (www.aegis.com/schools.asp). A copy of the webpage is attached as Exhibit F.

64. Upon information and belief, Aegis' false marking of its Zero-Tolerance Drug Testing product/service was done with the intent to deceive the public and induce the public to believe that Aegis' service was protected under the patent laws.

65. Pursuant to 35 U.S.C. §292, each day the web site was active should be considered a single offense. In the alternative, each "hit" on the web site should be considered a single offense.

RELIEF REQUESTED

WHEREFORE, Plaintiffs request that the Court enter a judgment in Plaintiffs favor and against Aegis and provide Plaintiffs the following relief:

A. Order, adjudge, and decree that Aegis has infringed the '788 Patent;

B. Order, adjudge, and decree that Aegis willfully and knowingly infringed the '788 Patent;

C. Order, adjudge, and decree that Aegis' infringement of the '788 Patent is exceptional under 35 U.S.C. § 285;

D. Issue preliminary and permanent injunctive relief prohibiting Aegis and their respective parents, subsidiaries, principals, officers, agents, affiliates, servants, attorneys, employees, and all others in privity with them from infringing the '788 Patent;

E. Order, adjudge, and decree that Aegis has infringed the '136 Patent;

F. Order, adjudge, and decree that Aegis willfully and knowingly infringed the '136 Patent;

G. Order, adjudge, and decree that Aegis' infringement of the '136 Patent is exceptional under 35 U.S.C. § 285;

H. Issue preliminary and permanent injunctive relief prohibiting Aegis and their respective parents, subsidiaries, principals, officers, agents, affiliates, servants, attorneys, employees, and all others in privity with them from infringing the '136 Patent;

I. Order, adjudge, and decree that Aegis has used unfair and deceptive practices that has caused Ameritox damages under Fl. Ann. Stat. §§ 501.201-213;

J. Order, adjudge, and decree that Aegis has tortiously interfered with Ameritox business relationships;

K. Order, adjudge, and decree that Aegis has falsely marked an advertised service on its web site in violation of 35 U.S.C. § 292;

L. Award Plaintiffs damages for patent infringement including prejudgment interest and costs against Aegis under 35 U.S.C. § 284;

M. Issue preliminary and permanent injunctive relief prohibiting Aegis and their respective parents, subsidiaries, principals, officers, agents, affiliates, servants, attorneys, employees, and all others in privity with them from engaging in unfair and deceptive practices under Fl. Ann. Stat. §§ 501.201-213;

N. Award Plaintiffs damages for injury caused by Defendant's tortious interference of business relationships;

O. Award Plaintiffs damages for Defendant's fraudulent misrepresentation;

P. Award Plaintiffs damages for Defendant's false marking of a non-patented process;

Q. Award Plaintiffs three times its damages to compensate Plaintiffs under 35 U.S.C. § 284;

R. Award Plaintiffs their reasonable attorneys' fees under 35 U.S.C. § 285; and

S. Award such other and further relief as the Court may deem just.

JURY DEMAND

Plaintiffs demand trial by jury.

Dated: December 21, 2007

Respectfully submitted,

AMERITOX, LTD. and U.D. TESTING, INC.

/s/ Michael R. Osterhoff
Michael R. Osterhoff

Michael R. Osterhoff, Esq.
BELL, BOYD & LLOYD, LLP
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Attorneys for Plaintiffs

EXHIBIT A

US005908788A

United States Patent [19]

Kell

[11] Patent Number: 5,908,788

[45] Date of Patent: *Jun. 1, 1999

[54] METHOD OF MONITORING PATIENT COMPLIANCE WITH MEDICATIONS PRESCRIPTIONS

[75] Inventor: Michael Kell, Atlanta, Ga.

[73] Assignee: U.D. Testing, Inc., Gainesville, Ga.

[*] Notice: This patent is subject to a terminal disclaimer.

[21] Appl. No.: 08/697,063

[22] Filed: Aug. 19, 1996

Related U.S. Application Data

[63] Continuation of application No. 08/248,102, May 24, 1994, Pat. No. 5,547,878, which is a continuation-in-part of application No. 08/145,821, Nov. 2, 1993.

[51] Int. Cl.[6] G01N 33/48

[52] U.S. Cl. 436/111; 436/171; 436/808; 436/901

[58] Field of Search 436/63, 111, 171, 436/808, 901

[56] References Cited

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Nilsson et al Effect of Urinary pH on the disposition of methadone in man EMBASE No. 82171209 W. Germany 1982.

Primary Examiner—Lyle A. Alexander

Attorney, Agent, or Firm—Kennedy,Davis & Kennedy,P.C.

[57] ABSTRACT

A method of monitoring compliance of a patient that has been placed on a medication maintenance program with a prescribed medication dosage by determining a normalized urine methadone concentration. An unadulterated urine sample is obtained from the patient. The urine methadone concentration and urine specific gravity are measured. The normalized urine medication concentration is calculated as a function of the measured medication concentration in the urine and the urine specific gravity. The calculated normalized urine medication concentration is compared with an expected medication concentration value for the patient for the maintenance program prescribed to determine any significant differences therebetween as an indication of noncompliance. Alternatively, a urinary-parameter normalized urine medication concentration is calculated as a function of the measured medication concentration in the urine, the urine specific gravity and at least one selected pharmacokinetic parameter of the medication. The calculated urinary-parameter normalized urine medication concentration is compared with an expected medication concentration value for an average compliant patient for the maintenance program prescribed to determine any significant differences therebetween as an indication of noncompliance.

8 Claims, 8 Drawing Sheets

FIG 1

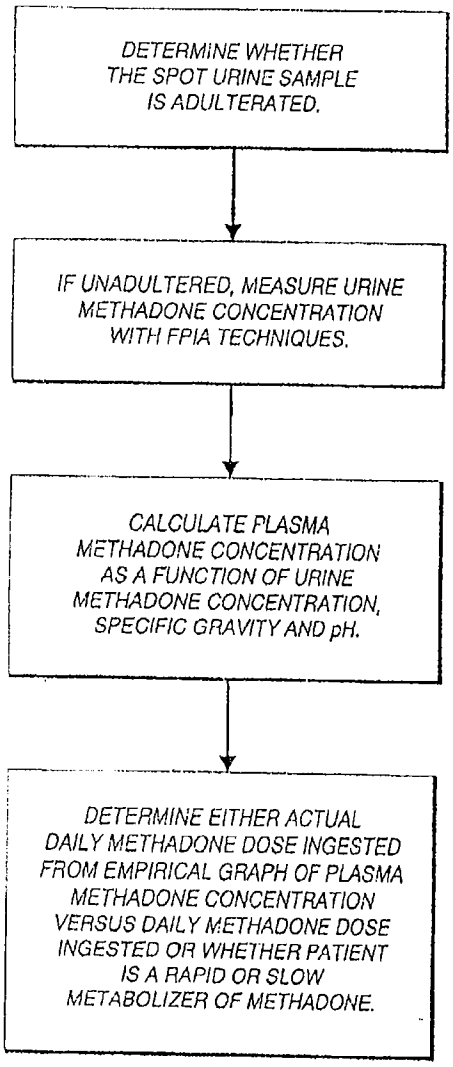
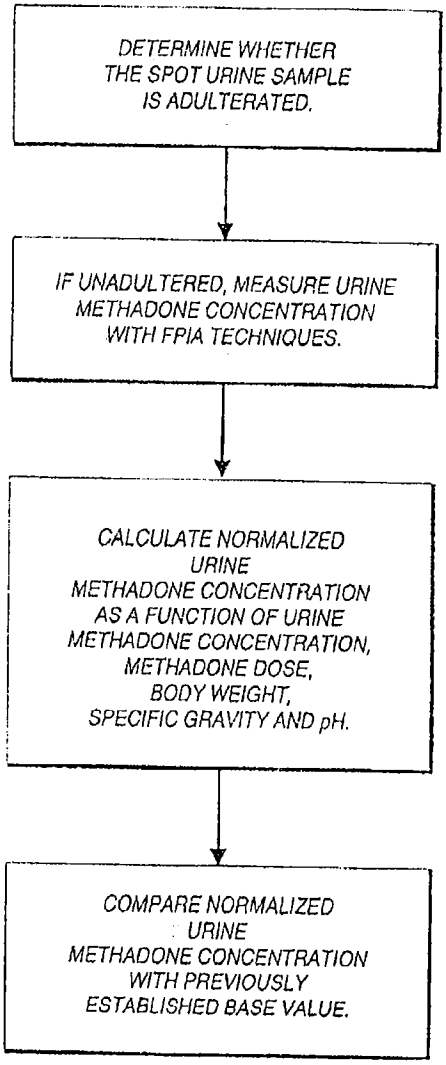

DETERMINE WHETHER THE SPOT URINE SAMPLE IS ADULTERATED.
IF UNADULTERED, MEASURE URINE METHADONE CONCENTRATION WITH FPIA TECHNIQUES.
CALCULATE PLASMA METHADONE CONCENTRATION AS A FUNCTION OF URINE METHADONE CONCENTRATION, SPECIFIC GRAVITY AND pH.
DETERMINE EITHER ACTUAL DAILY METHADONE DOSE INGESTED FROM EMPIRICAL GRAPH OF PLASMA METHADONE CONCENTRATION VERSUS DAILY METHADONE DOSE INGESTED OR WHETHER PATIENT IS A RAPID OR SLOW METABOLIZER OF METHADONE.

FIG 2


DETERMINE WHETHER THE SPOT URINE SAMPLE IS ADULTERATED.
IF UNADULTERED, MEASURE URINE METHADONE CONCENTRATION WITH FPIA TECHNIQUES.
CALCULATE NORMALIZED URINE METHADONE CONCENTRATION AS A FUNCTION OF URINE METHADONE CONCENTRATION, METHADONE DOSE, BODY WEIGHT, SPECIFIC GRAVITY AND pH.
COMPARE NORMALIZED URINE METHADONE CONCENTRATION WITH PREVIOUSLY ESTABLISHED BASE VALUE.

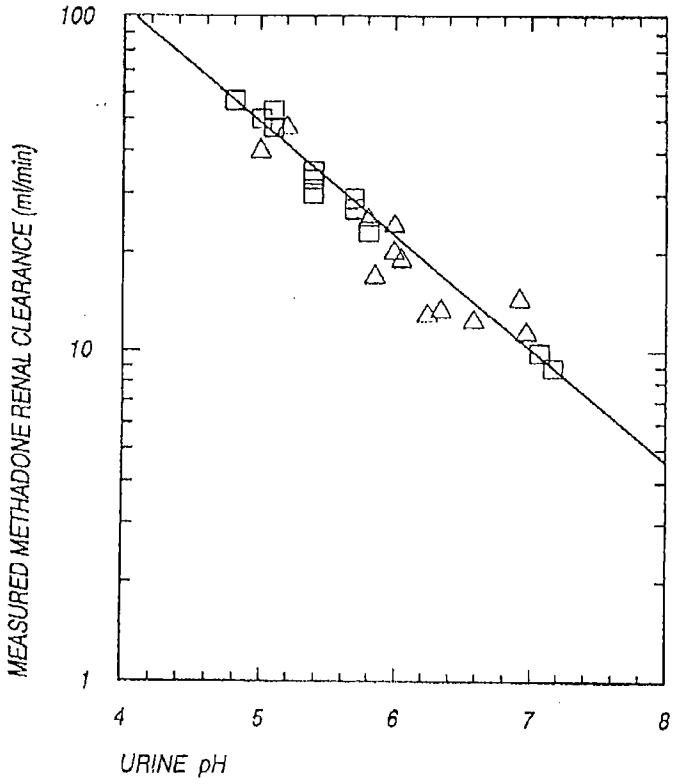

100
10
1
MEASURED METHADONE RENAL CLEARANCE (ml/min)
4
5
6
7
8
URINE pH

FIG 3

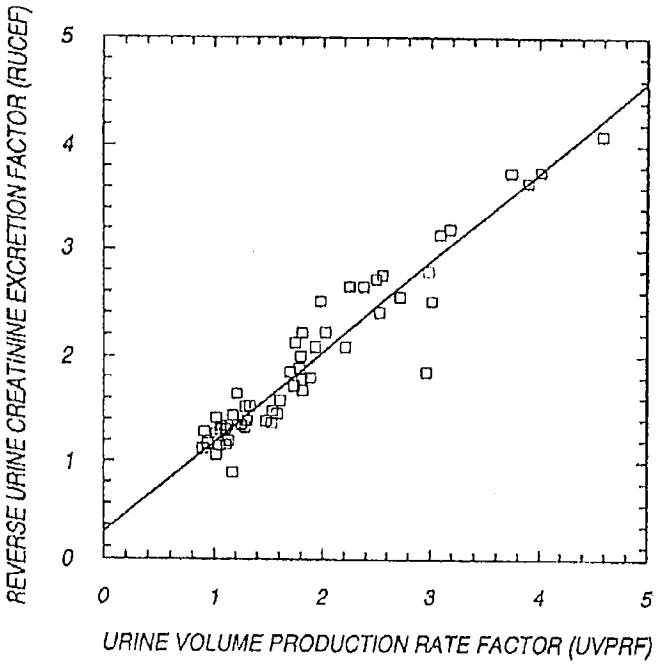

5
4
3
2
1
0
REVERSE URINE CREATININE EXCRETION FACTOR (RUCEF)
0
1
2
3
4
5
URINE VOLUME PRODUCTION RATE FACTOR (UVPRF)

FIG 4

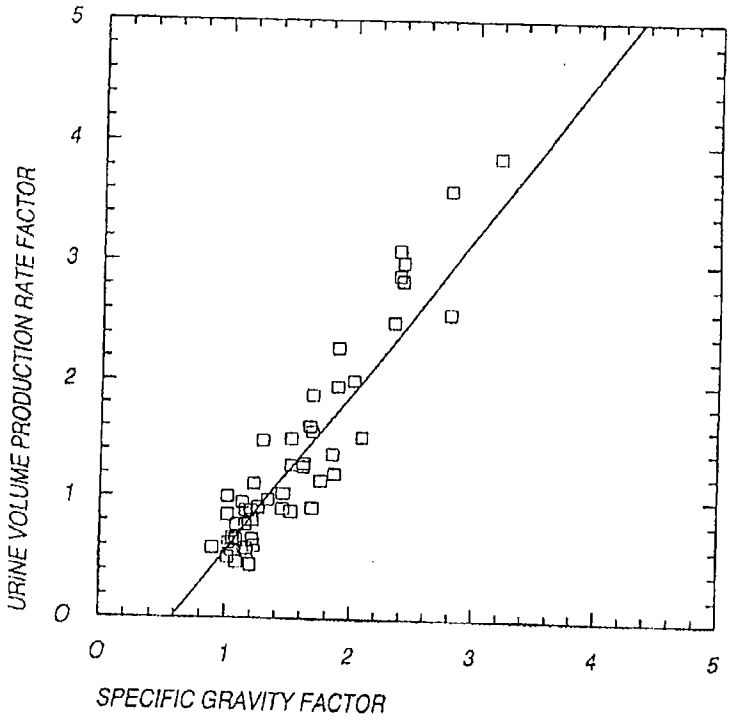

URINE VOLUME PRODUCTION RATE FACTOR
SPECIFIC GRAVITY FACTOR
0
1
2
3
4
5

FIG 5

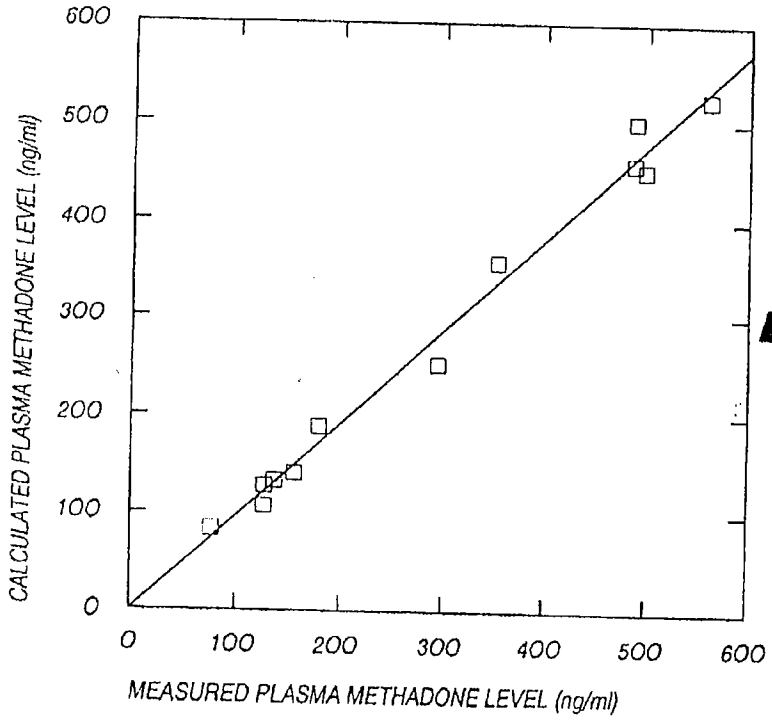

CALCULATED PLASMA METHADONE LEVEL (ng/ml)
MEASURED PLASMA METHADONE LEVEL (ng/ml)
0
100
200
300
400
500
600

FIG 7

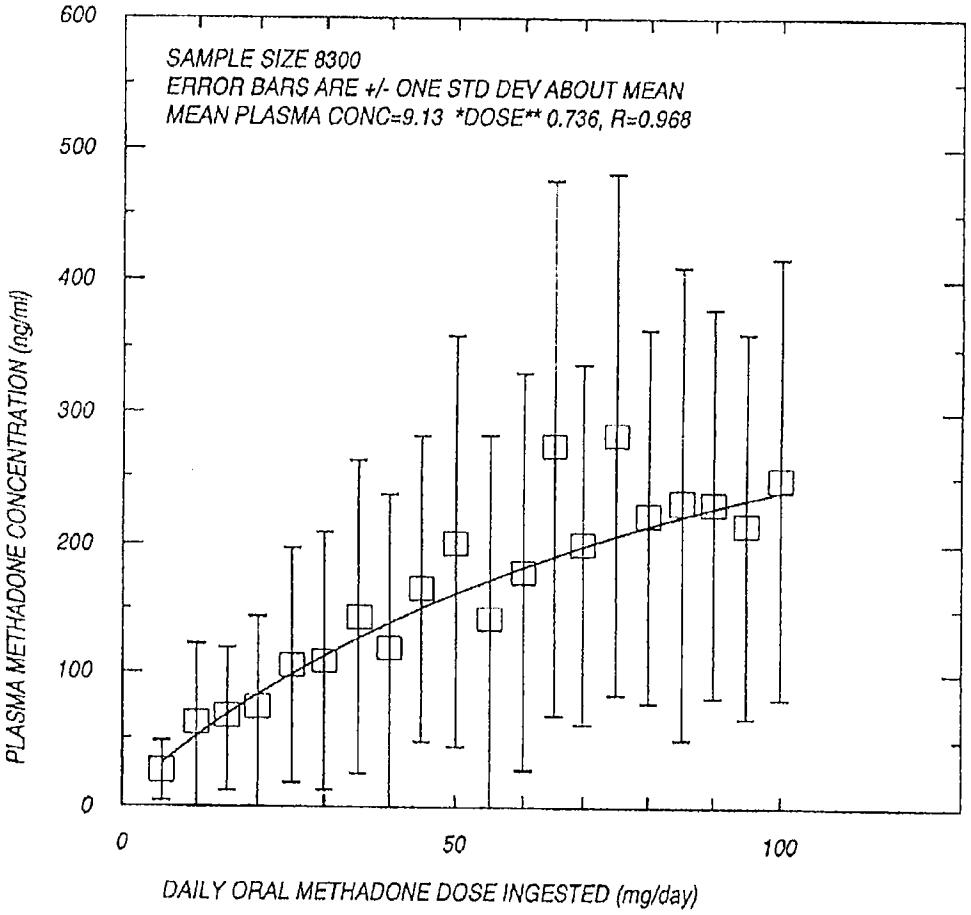

SAMPLE SIZE 8300
ERROR BARS ARE +/- ONE STD DEV ABOUT MEAN
MEAN PLASMA CONC=9.13 *DOSE** 0.736, R=0.968
PLASMA METHADONE CONCENTRATION (ng/ml)
600
500
400
300
200
100
0
0
50
100
DAILY ORAL METHADONE DOSE INGESTED (mg/day)

FIG 6

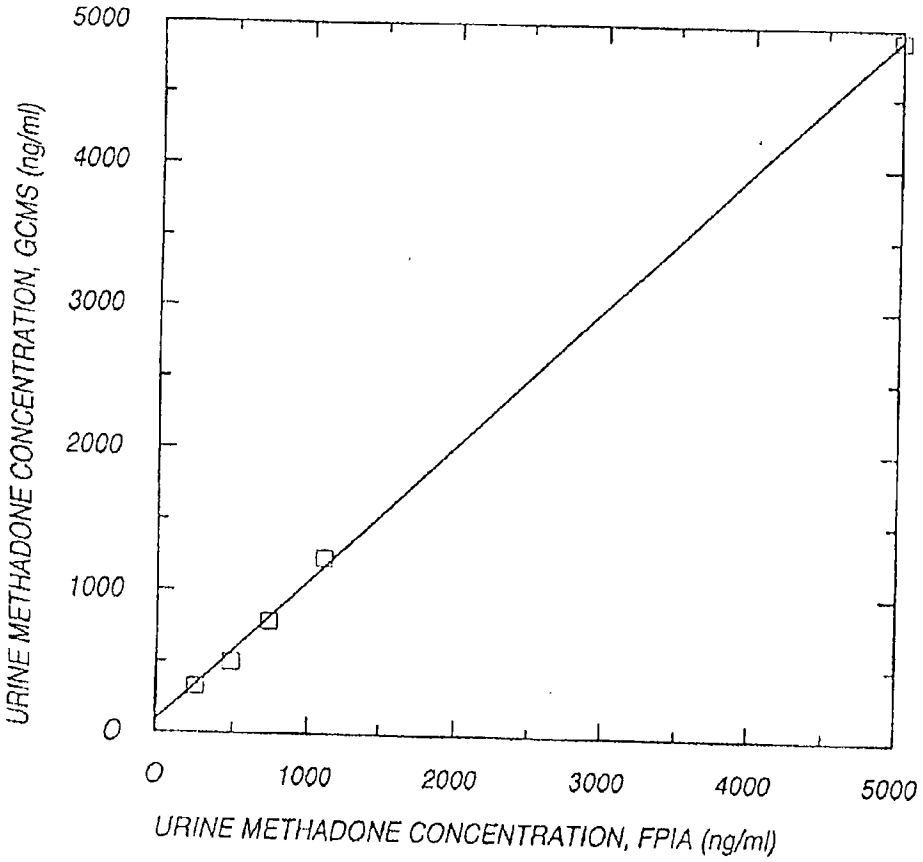
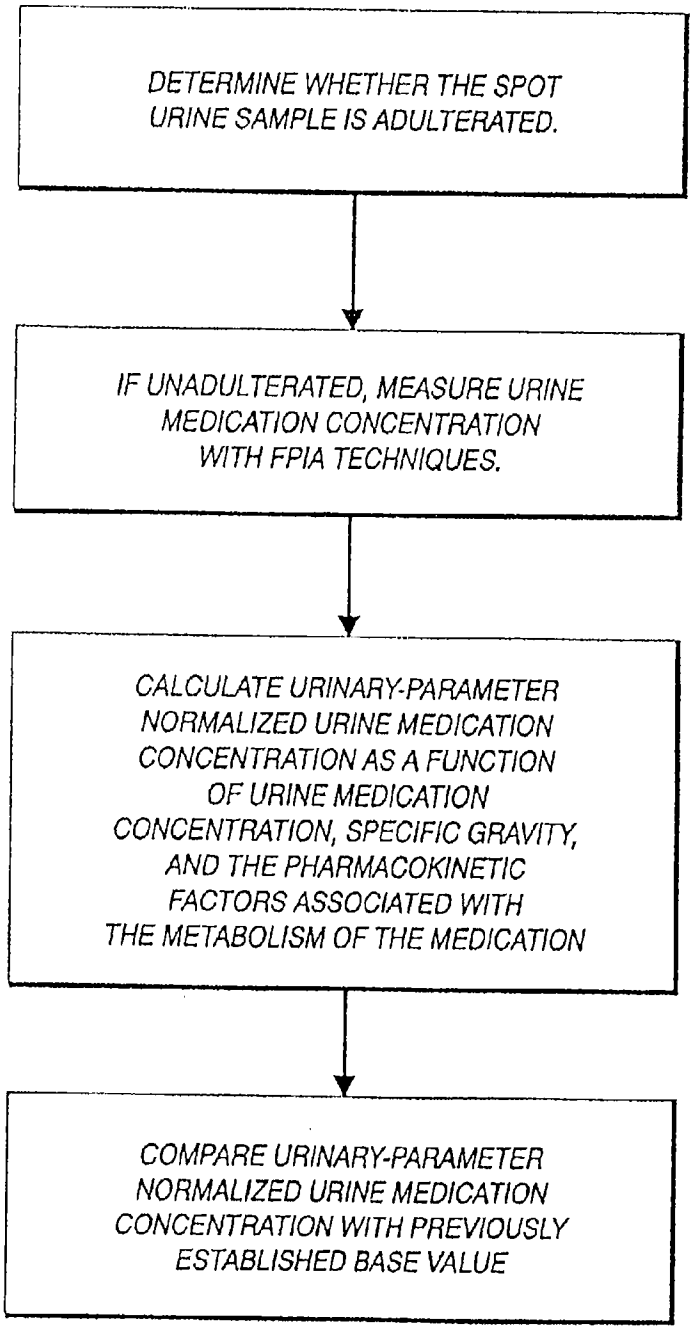

5000
4000
3000
2000
1000
0
URINE METHADONE CONCENTRATION, GCMS (ng/ml)
0
1000
2000
3000
4000
5000
URINE METHADONE CONCENTRATION, FPIA (ng/ml)

FIG 8

FIG 9


DETERMINE WHETHER THE SPOT URINE SAMPLE IS ADULTERATED.
IF UNADULTERATED, MEASURE URINE MEDICATION CONCENTRATION WITH FPIA TECHNIQUES.
CALCULATE URINARY-PARAMETER NORMALIZED URINE MEDICATION CONCENTRATION AS A FUNCTION OF URINE MEDICATION CONCENTRATION, SPECIFIC GRAVITY, AND THE PHARMACOKINETIC FACTORS ASSOCIATED WITH THE METABOLISM OF THE MEDICATION
COMPARE URINARY-PARAMETER NORMALIZED URINE MEDICATION CONCENTRATION WITH PREVIOUSLY ESTABLISHED BASE VALUE

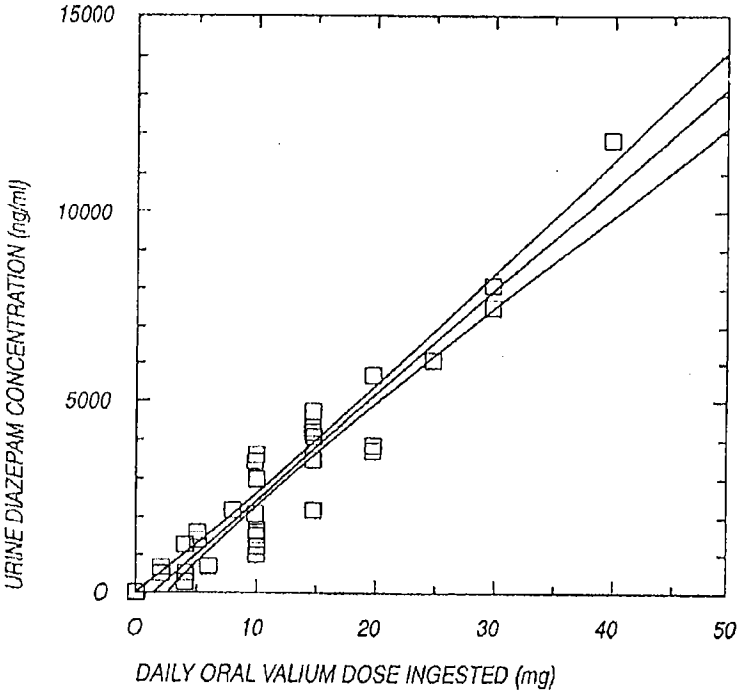

15000
10000
5000
0
URINE DIAZEPAM CONCENTRATION (ng/ml)
0
10
20
30
40
50
DAILY ORAL VALIUM DOSE INGESTED (mg)

FIG 10

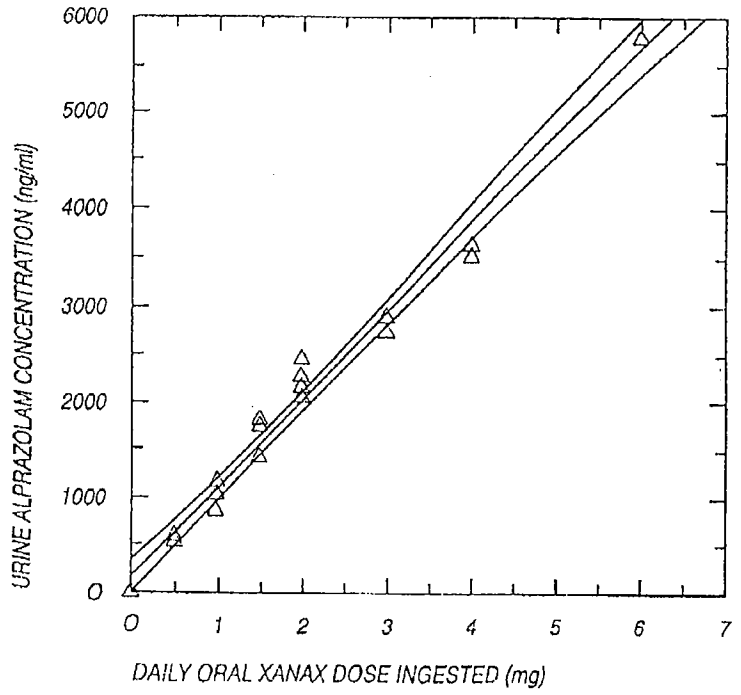

6000
5000
4000
3000
2000
1000
0
URINE ALPRAZOLAM CONCENTRATION (ng/ml)
0
1
2
3
4
5
6
7
DAILY ORAL XANAX DOSE INGESTED (mg)

FIG 11

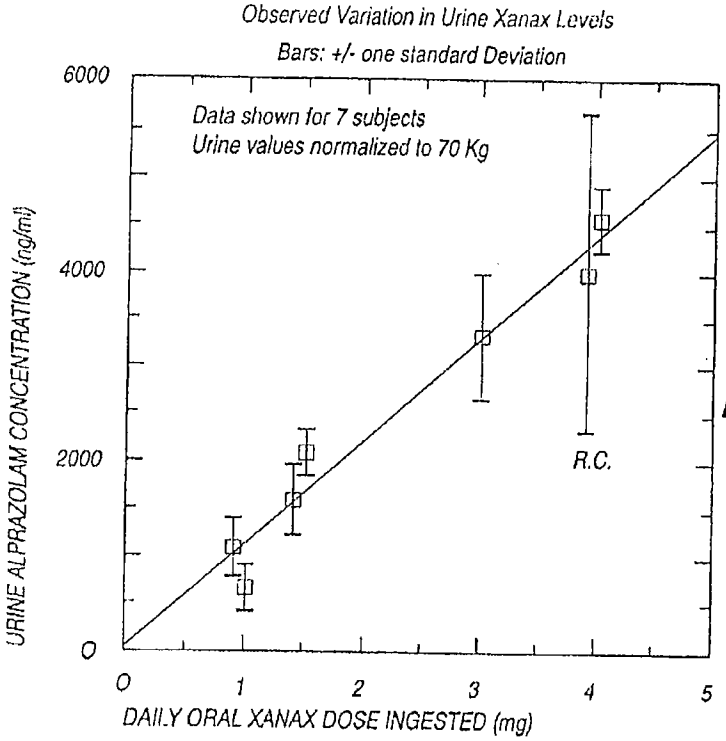

Observed Variation in Urine Xanax Levels
Bars: +/- one standard Deviation
Data shown for 7 subjects
Urine values normalized to 70 Kg
R.C.
URINE ALPRAZOLAM CONCENTRATION (ng/ml)
6000
4000
2000
0
0
1
2
3
4
5
DAILY ORAL XANAX DOSE INGESTED (mg)

FIG 12

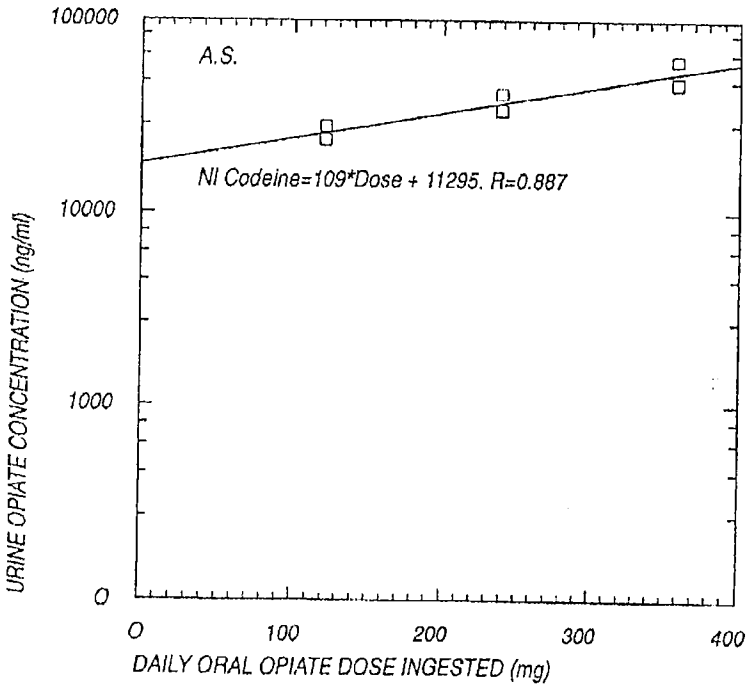

A.S.
NI Codeine=109*Dose + 11295. R=0.887
URINE OPIATE CONCENTRATION (ng/ml)
100000
10000
1000
0
0
100
200
300
400
DAILY ORAL OPIATE DOSE INGESTED (mg)

FIG 13

METHOD OF MONITORING PATIENT COMPLIANCE WITH MEDICATIONS PRESCRIPTIONS

REFERENCE TO RELATED APPLICATION

This is a continuation of application Ser. No. 08/248,102 filed on May 24, 1994 now U.S. Pat. No. 5,547,878 which is a continuation in part of Ser. No. 08/145,821 filed on Nov. 2, 1993.

TECHNICAL FIELD

The present invention relates to therapeutic drug ingestion monitoring. More particularly, the invention relates to methods of monitoring patients who are being prescribed potentially abusable or dangerous medications and have been placed on medication maintenance programs for compliance therewith.

BACKGROUND OF THE INVENTION

In the field of medicine and psychiatry, a number of medications, such as opioids, sedative-hypnotics, anticonvulsants, neuroleptics, and antidepressants, have been found safe and efficacious for the treatment of patients with biologically-based mental and physical illnesses. Patients placed on prescribed medication treatment plans are typically monitored. Subjective and objective methods are used to identify bothersome symptoms and to implement any changes necessary during the course of treatment. Monitoring generally continues for as long as treatment is provided. For example, the Hamilton Anxiety Scale can be used to quantify the amount of anxiety remaining as treatment proceeds. If the level of residual anxiety decreases significantly, say from the proper prescription of a benzodiazepine drug like diazepam, then the physician and patient can be assured that treatment is efficacious and should be continued.

Preferably both quantitative and analytical methods should be used to follow the patient on a repetitive basis to insure that the patient is indeed ingesting the prescribed amounts of medication in the proper manner and responding as expected. Currently, the most common method of monitoring patients for medication compliance is clinical observation which involves individual counseling and close personal supervision by physicians. Physicians observe physiological signs and symptoms such as intoxication, drug withdrawal typically occurring for benzodiazepines, barbiturates and opioids, or residual signs of illness such as tremor in anxiety, sighing in depression, and nociception in pain syndromes. Physicians also listen to patient complaints regarding degree of pain relief and evaluate psychological changes over time. This method however is time consuming, expensive and highly subjective. Needless to say, it is fraught with potential errors.

Additional compliance information can be obtained using qualitative urine monitoring methods such as the standard laboratory procedure called enzyme-multiplied immunoassay (EMIT). Utilizing an arbitrary cutoff value, these methods provide the clinician with a simple positive or negative indication of the possible presence or absence of a parent drug or its metabolites in a patient's urine. The parent drug is the prescribed medication itself and the metabolites are those chemical derivatives of the medication which naturally occur upon the patient's body metabolizing the medication. These tests do not provide information concerning the time or amount of last drug use or whether or not the prescribed dose of medication was ingested properly, diverted or supplemented.

Physicians utilizing only clinical evaluation and qualitative urine drug screening test results may develop problems in their treatment methods. Such is often the case in treating patients who have become biochemically dependent upon opioids either through prescription or illegal use. Opioid addicts experience great difficulty eliminating their dependency upon such drugs and typically enter into extended rehabilitative treatment programs which utilize prescribed methadone dosages to eliminate opioid dependency. Physicians must effectively assess the condition of patients on methadone maintenance programs in order to adjust dosages and monitor compliance. If a patient is continually testing positive for opioids or complains of continuing subjective opioid withdrawal symptoms, a physician may conclude that the currently prescribed dose of methadone is not sufficient to curb the body's desire for opioids and may increase the prescribed dosage. This highly subjective monitoring method can result in over-medication, patients being given more methadone than they require, creating an unnecessary reliance on methadone. Alternately, physicians sometimes conclude, erroneously, that a patient's methadone dose should be sufficient to prevent opioid withdrawal and drug cravings and deny the patient a further increase sufficient to stop illicit opioid use. Such action can expose the patient to further intravenous drug use and the associated negative social and medical consequences which can follow such as HIV, hepatitis, and blood poisoning.

Similar problems with treatment may arise for patients prescribed diazepam for longstanding generalized anxiety. Patients may not show improvement in their condition even though this therapy is known to be highly efficient. This medication is a member of the sedative-hypnotic family of benzodiazepines which have been clinically shown to cause sedation, hypnosis, decreased anxiety, muscle relaxation, anterograde amnesia and anticonvulsant activity. A patient, for example, may insist that he or she is ingesting the medication as prescribed, and yet claim no significant improvement in symptomology. The physician suspects that the patient is not ingesting the medication properly and perhaps is selling it, and orders a qualitative urine drug screen to verify compliance. The screen is reported as positive at greater than 200 ng/ml drug concentration. Since some benzodiazepine is present the physician assumes, incorrectly, that the patient is compliant, but will require additional medications and increases the daily dose. In truth, the patient is diverting the majority of his or her dose to the illicit market and only ingesting enough drug to test positive on the drug screen.

Patients also commonly visit multiple physicians to obtain similar medication for self-ingestion. These patients desire the intoxicating effects of the medication, but are unable to obtain sufficient quantities from a single source. Qualitative tests like the EMIT are generally not useful in detecting this situation since the quantitative amount of medication concentration in the body is not measured.

Another monitoring method sometimes used, though most often only in research centers, is direct measurement of parent drug concentrations or active metabolites concentrations of the drug in plasma. This method has been particularly useful to eliminate illicit opioid use of patients on methadone maintenance programs. It is known from analytical studies using venous blood samples obtained from stable patients that plasma methadone concentrations ranging from 150–600 ng/ml are necessary. This direct method is not very practical since it requires the use of time consuming, expensive, and highly technical analytical procedures such as high pressure liquid chromatography and

gas chromatography/ mass spectrometry since active and inactive metabolites must be quantified separately. Additionally, for many patients the obtaining of plasma samples is invasive, offensive and difficult due to inadequate venous access. Medical professionals must also be concerned about their own health safety in doing this since they are exposed to blood products from patient groups which can have a high prevalence of hepatitis and HIV infection. Therefore, such procedures are primarily conducted in research centers and not generally utilized in standard maintenance programs.

While providing useful information relative to patient status and treatment compliance, the clinical monitoring methods described above, i.e. clinical interviews with patients, direct plasma drug measurement and qualitative urine drug screening, have distinct drawbacks which limit their usefulness in extended treatment programs. Therefore, it is seen that a need remains for a better method of monitoring patients who have been placed on potentially abusable and dangerous maintenance medications for compliance therewith. To help prevent continued medication misuse and better optimize patient medication dose, it would be advantageous for patients to have a facile bodily fluid, such as urine, regularly and quantitatively monitored for the presence of the medication. Such a monitoring method would help physicians both in prescribing adequate doses of medication and in monitoring patients to insure that they were only ingesting the prescribed amounts. Obtaining a fluid sample like urine would not be invasive to the patient or a safety risk to the health care provider. Accordingly, it is to the provision of such improved methods that the present invention is primarily directed.

SUMMARY OF THE INVENTION

In co-pending application Ser. No. 08/145,821 it is disclosed that patients in methadone maintenance programs can be monitored for compliance by sampling and analyzing a patient's urine for methadone concentration as an indicator of plasma methadone concentration which in turn provides a correlation to methadone dose ingested. This information is used to monitor the patient's compliance with a prescribed methadone program and to establish the proper methadone dose. First, it is preferable to determine whether the urine sample is indeed from the patient in question and whether the urine sample is adulterated as by comparing urine pH, specific gravity, and creatinine level with that of normal urine and specific values previously determined for the patient. If found to be unadulterated and probably from the patient in question, the raw urine medication concentration is measured with standard quantitative laboratory methods. For example, the urine sample may be measured using high pressure liquid chromatography or gas chromatography/ mass spectrophotometry, but preferably by using fluorescence polarization immunoassay (FPIA) because of its ease and rapidity of analysis. FPIA is employed such as with an Abbott TDX or ADX Analyzer.

Once an analytical value has been determined for the actual concentration of methadone in the sample, adjustments are made to account for the effects of variations in certain urinary parameters upon this concentration. A relationship exists between the actual concentration of methadone adjusted for compounding effects of urine specific gravity, the renal clearance of methadone as a function of urine pH, and the concurrent plasma methadone concentration. By obtaining multiple urine samples from a patient, once or twice a week, it is possible to establish a stable, baseline, 24-hour trough plasma methadone concentration for each patient against which a current or future value can be statistically compared.

It was also disclosed that the actual urine methadone concentration can be converted to a urinary parameter-normalized urine methadone concentration. The calculation incorporates the measured actual urine methadone concentration, urine specific gravity, and the pharmacokinetic parameters associated with metabolizing methadone of methadone dose, patient's body weight, and urine pH. By establishing an individual's expected value for the urinary-parameter normalized urine methadone concentration, subsequent readings may be compared with the expected value to evaluate whether the patient is compliant with his or her prescribed dose.

It has now also been discovered that a patient's urine may also be analyzed for parent drug and its metabolites concentrations as a method of monitoring compliance with a prescribed medication dosage. (Hereinafter the term "medication concentration" and "parent drug concentration" shall also be understood to include their metabolites.) A normalized urine medication concentration (nu) is determined by a relationship discovered to exist between urine specific gravity and raw urine parent drug and its metabolites concentrations. A urinary-parameter normalized urine medication concentration (nu_p) may also be determined by the pharmacokinetic manipulation of the normalized urine medication concentration. Both nu and nu, are utilized once or repetitively for determining patient compliance with prescribed medication dosage.

The normalized urine medication concentration is a constant value for each patient and may be compared to an individual's expected nu once such is established or to a group of nu. The individual's expected nu is established by obtaining multiple urine samples from a patient once or twice a week and evaluating those samples for nu to obtain historical data on that patient. If the current nu is compared to and found to be similar to the expected nu, then the patient is deemed in compliance. This method of monitoring compliance is dependant upon the assumption that a patient is initially compliant in order to obtain the expected value.

In determining normalized urine medication concentration the urine is preferably first tested for adulteration in the same manner as discussed above. If found to be unadulterated, the urine methadone concentration is measured with standard quantitative laboratory methods, preferably FPIA. Once an analytical value has been determined for the raw concentration of medication in the urine sample, a normalized urine medication concentration is calculated in accordance with its relationship to specific gravity as hereinafter described.

Alternatively, for clinical situations the urinary-parameter normalized urine medication concentration is preferably utilized since an individual's expected value need not be established. Instead, the urinary-parameter normalized urine medication concentration is compared with an expected nu_p value of an average patient for the maintenance program prescribed. This method is particularly applicable for potentially abusable or dangerous medications such as antidepressants, anticonvulsants, beta-blockers, alpha agonists and antagonists, neuroleptics, analgesics, antirheumatics, and chemotherapy agents.

The nu_p is calculated by adjusting the normalized urine medication concentration for compounding effects of urine pH, medication dose, patient body weight, urine flow rate and other pharmacokinetic parameters associated with the metabolism of a particular drug. The expected nu_p value of

an average patient was established by obtaining numerous samples of controlled compliant patients on prescribed doses of medication and evaluating those samples for nu_p. If the current value of the nu_p is within ±20 percent of the nu_p value expected of the average patient on the same prescribed dose, the patient is considered to be in compliance with his or her prescribed dose.

Compliance may also be confirmed by using the current urinary-parameter normalized urine medication concentration to estimate the correlating daily medication dose from a previously developed empirical graph of urinary-parameter normalized urine medication concentration (ng/ml) versus daily oral medication dose ingestion (mg/day) for the general population. If the estimated daily medication dose is not the prescribed medication dose, then the patient is not in compliance.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a block diagram of a preferred method of the invention as it relates to a methadone maintenance program.

FIG. 2 is a block diagram of another preferred method of the invention as it relates to a methadone maintenance program.

FIG. 3 is a graph of measured methadone renal clearance versus urine pH.

FIG. 4 is a graph of reverse urine creatinine excretion factor (RUCEF) versus urine volume production rate factor (UVPRF).

FIG. 5 is a graph of urine volume production rate factor (UVPRF) versus specific gravity factor (SGF).

FIG. 6 is a graph of plasma methadone concentration versus daily oral methadone dose.

FIG. 7 is a graph of plasma methadone concentration calculated using the method of the present invention versus measured plasma methadone concentration using Abbott fluorescence polarization immunoassay (FPIA).

FIG. 8 is a graph of urine methadone concentrations simultaneously measured by FPIA and gas chromatography/mass spectrometry (GC/MS).

FIG. 9 is a block diagram of a preferred method of the present invention as it relates generally to monitoring medication maintenance programs.

FIG. 10 is a graph of urinary-parameter normalized urine diazepam concentration versus daily oral valium dose ingested.

FIG. 11 is a graph of urinary-parameter normalized urine alprazolam concentration versus daily oral xanax dose ingested.

FIG. 12 is a graph of urinary-parameter normalized urine alprazolam concentration versus daily oral xanax dose ingested showing patient standard deviations and mean levels.

FIG. 13 is a graph of urinary-parameter normalized urine opiate concentration for codeine versus daily oral medication dose ingested.

METHADONE MAINTENANCE PROGRAMS

For methadone maintenance programs, the optimum 24-hour trough plasma methadone concentrations is between 150–600 ng/ml, which has been generally recognized in past studies as most effective in deterring illicit opioid use. A patient's 24-hour trough plasma methadone concentration, as calculated by the present method, is compared to a previously developed empirical graph of plasma methadone concentration (ng/ml) versus daily oral methadone dose ingestion (mg/day) for the general population. The graph, as shown in FIG. 6, represents the 24-hour trough plasma methadone concentration expected for the average patient comprising the cohort from which the general population data was generated. The comparision helps a physician determine both how the patient is metabolizing methadone, what the most likely final methadone dose will be to attain the 150–600 ng/ml level, or whether the patient is compliant with his or her prescription.

Over time, a unique plasma concentration-daily methadone dose relationship is derived for each individual patient which can be compared to the relationship expected for that particular patient or for an average patient. If the two relationships are not similar, the patient's metabolism rate may account for any over- or under-effectiveness of the prescribed dose. A physician, in accounting for the patient's individual metabolism rate, can now optimize the patient's methadone dose to achieve an efficacious and safe plasma methadone concentration. Further, once the optimum methadone dose is established for the patient, the physician can monitor the patient for compliance with his or her prescribed dose by comparing the plasma methadone concentration of methadone, as calculated by the present method, with his expected, historical plasma methadone concentration for that particular methadone dose to reveal any covert methadone diversion or supplementing.

Testing for Adulteration

First, a supervised, spot sample of urine is collected from a patient. Several properties of the urine are measured to evaluate whether the urine is adulterated, adulteration being the altering by a patient of his or her urine in an effort to prevent detection of illicit drug use or diversion of methadone. Adulteration typically is accomplished by adding foreign substances to the urine such as salt, bleach, or vinegar. Many patients attempt to dilute amount of drugs in the urine sample by drinking large quantities of water or by adding water to the sample. Adulteration may also occur by substituting another person's urine for the patient's own urine, including instillation of foreign urine into the patient's bladder.

In checking for adulteration, urine pH is measured, as with the use of a pH Data Logger type meter available from Oakton, to see if it is within the normally expected pH range of 4.5 to 8.5. Urine specific gravity is also measured to see if it is within the normal range of 1.004 to 1.035 units. A Digital Urinometer by Biovation may be used for this test. Creatinine, an end product of glycine and arginine metabolism excreted through the kidneys, is measured to evaluate renal function. The creatinine level in human urine usually ranges from 8 to 500 mg/dl, the range being affected by variables such as age, sex, diet, lifestyle and geographic location. Creatinine levels generally are homeostatically maintained by the body at a constant value for each individual patient over his or her lifetime. Creatinine levels may be determined on many different analyzers, including a TDx REA Creatinine System available from Abbott Laboratories. All of these tests are helpful in establishing normally expected ranges for each patient and the overall population of patients.

Once pH, specific gravity, and creatinine level values for the spot urine sample are obtained for a particular patient, comparisons can be made between the sample in question and values previously measured (if already available) both for the patient and for normals to ascertain whether the urine

sample is adulterated. If no adulteration is found, a data base is created or extended for the patient so that a basis of comparison exists for future spot urine samples. Of the three measures, urinary creatinine level is generally the most useful indicator as to whether the spot sample is that of the patient or of someone else.

Determination of Raw Urine Methadone Concentration

The unadulterated sample is next analyzed for raw urine methadone concentration, preferably using fluorescence polarization immunoassay (FPIA) technology. In this regard an Abbott TDX or ADX Analyzer may be profitably employed. Other standard analytical methods may also be used such as chromatography or other types of immunoassay. The value obtained is the raw urine methadone concentration, u.

Determination of Plasma Methadone Concentration

Plasma methadone concentration is obtained from the raw urine methadone concentration by utilizing a standard dimensionally correct relationship known as the renal clearance, which is,

$$cl=(u\cdot v)/p \tag{1}$$

where cl is renal clearance (ml/min), u is raw urine methadone concentration (ng/ml), v is the volume of urine collected in time (ml/min) or otherwise known as the urine volume production rate, and p is the measured plasma methadone concentration at the midpoint of the collection period (ng/ml).

Since the actual, current renal methadone clearance is not generally known for any one patient, nor can it easily be directly measured under normal clinic conditions, it must be estimated from an empirical relationship. From experiments measuring urine and plasma methadone concentrations over timed collection periods (which recognizes that the renal clearance for methadone is strongly affected by urinary pH because of the weakly basic properties of methadone), it has now been found that renal clearance relates to urine pH in the range 4.8–8.7 (see FIG. 3) as,

$$cl=104{,}228\cdot pH^{(-4.36)} \tag{2}$$

and for which generally, a strong dependence upon actual patient weight is not noticed.

Rearranging Equation (2), the plasma concentration of urine may be calculated as follows,

$$p=u\cdot v/cl \tag{3}$$

The actual, raw urine methadone concentration is known from the FPIA results. Renal clearance can be calculated from Equation (2) by utilizing the urine pH previously measured in testing for adulteration. However, actual values of the urine volume production rate, v, are not available since routine clinical urine sampling procedures only provide a point-in-time or spot urine sample.

Heretofore, it has been thought to be impossible to calculate plasma methadone concentration of a drug from the spot urine sample and that a timed urine collection must be done (usually 24 hours). It has now been found that these beliefs are flawed.

It is now appreciated that renal excretion rates (mg/min) for drugs and urine metabolites are relatively constant for any patient during a typical day. This constancy has now been experimentally verified by examining the renal excretion rates of methadone, benzodiazepines, other drugs and creatinine and other endogenous metabolites as a function of urine volume production rate. For example, sequential, complete and timed (1–8 hours holding periods) aliquots of urine for 12 compliant control subjects were collected over 24 to 72 hour periods. For each and every urine aliquot, urine volume production rate (ml/min), specific gravity and creatinine concentration (ng/ml) were determined.

Using this data, a dimensionless, linear relationship was found to exist that is the same for all patients, between a urine volume production rate factor (UVPRF) and a reverse urine creatinine excretion factor (RUCEF). For each individual, control, urine collection period, the UVPRF is defined by the ratio of urine volume production rate for each urine aliquot collected, v, to the urine volume production rate for the most concentrated sample in the collection period with a specific gravity usually near 1.030, v',

$$UVPRF=v/v' \tag{4}$$

The RUCEF factor is defined by the ratio of the creatinine concentration of the most concentrated urine aliquot with a specific gravity usually near 1.030, u', to the creatinine concentration for each urine aliquot collected, u,

$$RUCEF=u'/u. \tag{5}$$

This linear relationship is shown in FIG. 4. The best fit linear regression line is given by the expression,

$$RUCEF=0.942(SE\ 0.013)\cdot UVPRF+0.121(SE\ 0.043) \tag{6}$$

$$u'/u=0.942\cdot v/v'+0.121 \tag{7}$$

adjusted squared multiple R=0.985, standard error (SE) of estimate=0.242, F-ratio 4965.,

Therefore, contrary to the traditional teachings of those skilled in the art, urine drug and metabolite concentrations, u, are inversely related to the volume of urine produced by the kidneys, v, clearly demonstrating that the product (u·v) is constant at any particular time point and urine pH (given a steady-state plasma methadone concentration p and renal clearance cl).

Since p, cl, and (u·v) at any time point and urine pH are constant, steady-state values,. it follows that from Equation (7) some empirical mathematical relationship must exist between u and v such that given an arbitrary urine volume production rate v' and an equivalent u' at a reference point (specific gravity 1.030):

$$(u\cdot v)_{sg\ actual}=(u'\cdot v')_{sg\ 1.030} \tag{8}$$

or upon rearrangement for u' gives,

$$u'=u\cdot(v/v') \tag{9}$$

where the products given in Equation (9) are those measured for a spot urine collected with an actual specific gravity and a corrected specific gravity typical of a morning void of 1.030.

Using controlled urine collections, a urine volume production rate v' of 0.44 ml/min for persons with reasonably normal renal functions at a specific gravity of 1.030 was measured. It has also been discovered that a linear relationship exists between the urine volume production rate factor and the specific gravity factor (SGF), {(1.030–1.000)/(sg–1.000)}, as shown in FIG. 5 and given as follows:

$$UVPRF=v/v'=2.43(SE\ 0.106)\cdot SGF-1.43(SE\ 0.216) \tag{10}$$

where the adjusted squared multiple R=0.856, standard error of the estimate=0.787, F-ratio 482.

Combining all of the above considerations, plasma methadone concentrations can be calculated by substituting Equations (2, 8, 9 and 10) in Equation (3):

$$p = u \cdot v/cl = u' \cdot v'/cl \quad (11)$$

$$= v' \cdot u \cdot (v/v')/cl$$

$$= 0.44 \cdot u \cdot (2.43 \cdot SGF - 1.43)/104{,}218 \cdot pH^{(-4.76)}$$

where values of u, specific gravity, and pH are known from previous test results on a patient's spot urine sample. The equation may be more generally expressed as follows:

$$p = k_3 \cdot u \cdot (k_1 SGF - k_2)/k_4 \cdot pH_{(-k5)} \quad (11a)$$

wherein k_3 is a constant approximately equal to 0.44, k_1 is a constant equal to 2.43, k_2 is a constant equal to 1.43, k_4 is a constant equal to 104,218 and k_5 is a constant equal to 4.76.

Comparing Patient's Calculated Plasma Methadone Concentration to that of an Average Patient for the Same Dose

Once the plasma methadone concentration is calculated from Equation (11), it is compared with the plasma methadone concentration expected from an average patient on a similar daily methadone dose as shown in FIG. 6, which demonstrates how plasma methadone concentration varies with dose for the standard population. FIG. 6 was developed by utilizing data from 8300 urine samples from 150 methadone maintenance patients on controlled daily methadone dosages.

Using this figure, a clinician can estimate how a prescribed dose will effect a patient's methadone plasma level. For example, a patient on a 70 mg/day methadone dose is expected from FIG. 6 to have a plasma methadone concentration of 200 ng/ml. However, from the spot urine sample the calculated plasma methadone concentration is 100 ng/ml thereby indicating that the patient's body is quickly metabolizing the methadone and a higher dose is needed or that the patient is diverting the methadone to others or that the patient is simply not using it. Higher concentrations per dose suggest the opposite of the above. Knowing that the plasma methadone concentration does not correlate to the prescribed methadone dosage, the clinician now has valuable information to evaluate the next step in the patient's program.

An optional use of the calculated plasma methadone concentration is for estimates of the methadone doses that a patient has taken. FIG. 6 is used to estimate the patient's methadone dose by adjusting the calculated plasma methadone concentration relative to any parameters of the patient that fall outside the average patient parameters, such as patient body weight, methadone plasma half-life, and time of ingesting dose.

Verification of Plasma Methadone Concentration Equation (11)

In order to ascertain the effectiveness of the plasma methadone concentration formulation, blood and urine samples were taken from a control group of patients. Urine and blood samples were simultaneously analyzed for plasma methadone concentration using FPIA and GC/MS. The urine methadone concentration was converted to a calculated plasma methadone concentration utilizing the formulation of the present invention in Equation (11).

Referring now to FIG. 7, the accuracy of calculating plasma methadone concentration from urine methadone concentration is verified by the excellent linear agreement between the plasma concentrations calculated by the present method from random, spot urine measurements and concurrently measured plasma methadone concentrations using actual blood samples: Estimated=0.970 (SE 0.034) ·Measured−1.25 (SE 11.495), adjusted squared multiple R=0.987, standard error of estimate=20.155, F-ratio 810.

Determination of Urinary-Parameter Normalized Urine Methadone Concentration

The parameters of a patient's urine, such as pH and specific gravity, vary from one day to the next dependant upon the type and quantities of foods and beverages ingested. Additionally, individuals metabolizes these substances, as well as methadone, at different rates. To account for these variations, a urinary-parameter normalized urine methadone concentration, nu_p, is calculated that adjusts measured raw urine methadone concentration, u, in accordance with a prescribed methadone dose, urine specific gravity, patient's current body weight (lbs) and urine pH. The relationship between u, pH, dose and specific gravity was empirically developed using nonlinear regression analysis. Results were normalized to a dose level of 80 mg/day, a patient weight of 154 pounds, and urine pH of 6.5 giving the final equation for monitoring a patient's nu_p in Equation (12) as follows:

$$nu_p = (80/DOSE)^{0.823} \cdot (6.5/pH)^{-4.838} \cdot (BODY\ WEIGHT/154) \cdot UVPRF \cdot u$$

The equation may be generally expressed in Equation (12a) as follows:

$$nu_p = (k_8/DOSE)^{k_9} \cdot (k_5/pH)^{-k_6} \cdot (BODY\ WEIGHT/k_7) \cdot u \cdot (k_1 \cdot SGF - k_2)$$

wherein k_8 is a constant equal to 80, k_9 is a constant equal to 0.823, k_5 is a constant equal to 6.5, k_6 is a constant equal to 4.838, k_7 is a constant equal to 154, k_1 is a constant equal to 2.43 and k_2 is a constant equal to 1.43.

The urinary-parameter normalized urine methadone concentration is statistically constant and unique for each patient regardless of an individual's methadone metabolism and daily changes in urine parameters. Thus, a patient's expected nu_p, once established accurately for an individual patient within a statistical margin of error, may be used to evaluate methadone diversion or supplementation in patients by comparing subsequent calculations of nu_p with the patient's particular expected value of nu_p. If the subsequent calculation is similar to the expected value, the patient is complying with his prescribed dose.

The generation of a patient's nu_p expected value is done using standard statistical techniques developed for relating the mean and standard deviation observed from a particular sampling distribution (of size n elements) to the mean and standard deviation expected for the whole population of values, both for each patient and the population of all patients. For further details one can refer to the text, *Hahn G J, Meeker W Q, Statistical Intervals, John Wiley and Sons*, 1991.

To utilize such techniques it is first necessary to determine what the expected standard deviation is for the whole population of compliant patients under observation. Previously, it had been observed that although mean values for nu_p are different for each patient, the observed variability about the mean for compliant patients is quite consistent and similar to the overall cohort of compliant patients; suggesting that the following statistical technique can be utilized.

Sequential, urine data was retrieved from computer files for 216 patients (13,000 data points) and transferred into a commercial statistical/graphical package produced by Systat, Inc. Each patient's data was sorted individually by ascending concentration for initial data review. All data points having unusual creatinine values <10 or >500 mg/dl or a methadone concentration <300 or >60,000 ng/ml were discarded as being suspect and non-physiologic. Additional outliers were eliminated from each patient file using manual review (preliminary statistic data were available as a guide). For statistical reasons, all patients having less than 10 acceptable data points were also eliminated.

Using the remaining data sets for each patient (180 persons, approximately 12,000 individual urine values), individual nu, values were obtained from which individual means and standard deviations were calculated.

Utilizing this data, a plot of sample size (for each patient) versus calculated sample standard deviation (for each patient) was generated. Approximately, 180 individual, standard deviations (y-axis) were plotted against samples sizes ranging from 10 to 200 (x-axis). Using standard 95% confidence limit tables from *Hahn and Meeker*, lower and upper limits were co-plotted on the above curve by adjusting the overall population standard deviation until the data bounded by the prediction curves enclosed all acceptable data. The average population standard deviation for the set of acceptably, compliant patients was found to be about 3000 for this particular set of patients, though it could be lower if further restrictions to the initial data set were applied. In general, the average population standard deviation varies linearly with mean nu_p, and considering this effect the acceptable range for a particular patient can be narrowed.

Given this value, another set of prediction equations specifying the allowable range for the next measured nup for a particular patient, given a sample size of n, a mean nu_p for an individual patient and either the patient standard deviation or the population standard deviation (whichever is least), can be calculated as shown in *Hahn and Meeker*. If the measured value is within the acceptable statistical range, given a previously calculated mean and standard deviation, then it is accepted. If the value is too high or too low, this is marked on the urine drug screen under the column called Pred, as shown in clinical cases #'s 4 and 5, Tables F and G.

An alternative method which can be used to establish outliers for each patient data set, which is also statistically sound, is based upon the ratio of the currently determined nu_p to the mean nu_p calculated from previous values for an individual (usually a minimum of 3 to a maximum of 12, though any larger number of samples could be used.) By plotting log normal histograms of these calculated ratios for the same patient data set mentioned above, the expected variation about the most common value of unity for the entire population is determined. Ninety-nine percent confidence limits are distributed in a skewed manner about the value unity and range between about 0.43 to 2.30. Therefore, given a current mean nu_p for a particular patient, the acceptable values can be found by simple multiplication using 0.43 times nu_p for the lower limit and 2.30 times nu_p for the upper limits. Other confidence intervals are easily determined as well.

Verification of Urinary-Parameter Normalized Urine Methadone Concentration Equation (12)

Shown in Table A is a partial representation of data from a standard computer printout for a compliant patient in which is summarized both urine parameters and methadone concentrations. The last column in the figure represents the urinary-parameter normalized urine methadone concentration values for the patient which are quite constant once sg, pH, dose corrections are made to the raw urine methadone concentration. CR represents the specific gravity corrected urine creatinine concentration which should have a CV of less than 15 percent.

TABLE A

Date	Dose	Temp	pH	SG	CR	u	p	nu_p
04-20-92M	70	98.0	5.40	1.022	335	6838	167	6966
04-15-92W	70	96.0	5.70	1.024	268	6536	176	7381
04-13-92M	70	96.0	5.90	1.019	271	5462	259	10913
04-10-92F	70	98.0	5.70	1.021	377H	5180	177	7430
04-06-92M	70	98.0	5.90	1.028	261	7398	171	7208
04-02-92h	70	96.0	5.70	1.026	271	5990	149	6254
03-30-92M	70	94.0	5.60	1.021	303	4203	132	5532
03-25-92W	70	98.0	5.20	1.021	271	8469	187	7790
03-24-92T	70	98.0	6.00	1.023	243	3736	139	5852
03-20-92F	70	98.0	5.80	1.024	272	5601	164	6881
03-16-92M	60	94.0	5.30	1.022	286	7049	157	7448
03-13-92F	60	96.0	5.70	1.019	277	4935	199	9473
				Mean:	287	5950	173	7427
				SD:	35	1372	33	1492
				CV:	12.2	23	19.0	20
				Tests:	12	12	12	12

Clinical Examples

Case #1

J. S. is a 52 year old woman with right-sided, migraine headaches with aura beginning after her hysterectomy at age 44 and prior to regular use of any medication. Her migraines began with flashes of light and blurry vision in either eye. Often "a film covers my right eye." Prodromata was usually followed by right retro-orbital pain accompanied by photophobia and nausea. This patient also suffered tension headaches and headaches secondary to allergic rhinitis. She was able to clinically differentiate migraine and tension components of her headaches, as the migraine component was refractory to multiple trials of ergot alkaloids, benzodiazepines, NSAIDs, beta-blockers, calcium channel blockers and psychotherapy. Multiple CT scans had been normal.

J. S. had been biochemically dependent upon prescription opioids to relieve migraine pain for over a year prior to her

referral to a methadone maintenance clinic. According to Federal Register 21 CFR Part 291, a person biochemically dependent (this is the current definition for opioid dependency utilized by the federal government) to narcotics for more than a year qualifies to enter into a methadone maintenance program.

J. S.'s situation was similar to that of approximately 0.5% of the general, adult population of the United States who are also biochemically dependent upon opioid medications because of legitimate medical illness and disease. Oftentimes, it is difficult for the clinician to determine whether or not the patient is currently using opioids for relief from organic pain or is treating the psychological sequelae of their disability. In either case, methadone maintenance was the most efficacious choice to help and protect the patient.

J. S. enrolled in the methadone maintenance program 36 months ago for pain management. Gradual titration to 45 mg of methadone was achieved over a short time period during which migraines slowly decayed in frequency and severity. During her time in treatment she had subsequently suffered only 2 migraine attacks which were greatly reduced in intensity. Both attacks were related to a transient decrease in plasma methadone levels below 80 ng/ml secondary to vomiting associated with viral syndromes.

A urine history is shown in Table B for this patient showing both estimated plasma methadone levels and the urinary parameter-normalized methadone concentration.

TABLE B

Date	Dose	Temp	pH	SG	CR	u	p	nu_p
07-01-93h	45	94.0	7.70	1.012	319	1069	348	21153
06-21-93M	45	94.0	6.90	1.008	265	1336	401	25720
06-14-93M	45	94.0	6.60	1.011	273	2109	368	22145
06-07-93M	45	95.0	7.30	1.011	270	1883	399	32208
06-03-93h	45	98.0	7.00	1.010	254	646	168	10174
05-27-93h	456	94.0	7.60	1.018	269	1246	215	13051
05-20-93h	45	95.0	6.80	1.011	275	1285	259	15585
05-13-93h	45	95.0	7.80	1.011	272	757	293	17845
05-03-93M	45	97.0	5.50	1.020	357H	4094	153	7585
04-29-93h	45	94.0	6.70	1.014	N/T	1318	180	10815
04-22-93h	45	96.0	6.80	1.020	320	3900	335	20168
04-12-93M	45	94.0	7.20	1.009	260	915	310	18777
				Mean:	285	1713	285	17265
				SD:	32	1146	90	5439
				CV:	11.3	66.8	31.2	31.5
				Tests:	11	12	12	12

Case #2

A. N. is a 44 year old woman whose migraine with aura began approximately 20 years ago. Beginning with blurred vision, subsequent unilateral headaches were invariably accompanied by nausea and vomiting, photophobia, and hypersensitivity to motion of her head and to cigarette smoke. Despite trials of biofeedback, physical therapy, and medications (trials of beta blockers, calcium channel blockers, ergot alkaloids over the years) and drug holidays; the frequency of her headaches had increased over the years to nearly daily occurrence. Lumbar punctures and multiple CT and MRI scans of her head were normal.

Following failure of self-administered IM administration of nalbuphine to control her pain, she began methadone maintenance 24 months ago. Because of many years of prior use of barbiturate-containing compounds her hepatic metabolic function was significantly enhanced requiring more than normal amounts of methadone—as shown by urine plasma concentration estimates. After stabilization on 130 mg per day of methadone, her migraines ceased completely at a plasma methadone level above 135 ng/ml. She continued to experience infrequent stress-related headaches, which were slowly decreasing in severity and frequency.

Urine histories are shown for this patient in Tables C and D. Notice how plasma methadone levels had increased in this patient over time as hepatic function returned to normal by discontinuing barbiturate-containing compounds (bar).

TABLE C

Date	Dose	Temp	pH	SG	CR	bar	u	p	nu_p
06-01-91S	100	N/T	5.10	1.021	200	HI	6338	127	3243
05-29-91W	100	N/T	5.40	1.021	184	2370	1985	52	1339
05-25-91S	100	N/T	5.40	1.020	N/T	N/T	1360	39	995
05-22-91W	100	N/T	5.10	1.013	N/T	N/T	1511	62	1582
05-20-91M	100	N/T	5.10	1.005	134	HI	615	80	2026
05-18-91S	100	N/T	5.40	1.017	N/T	N/T	2367	76	1952
05-15-91W	80	N/T	5.40	1.019	129	HI	1120	35	1070
05-13-91M	65	N/T	5.70	1.009	72	HI	335	37	1367
05-11-91S	65	N/T	5.10	1.016	182	HI	816	25	911
05-08-91W	50	N/T	5.40	1.010	N/T	N/T	853	65	2924

TABLE C-continued

Date	Dose	Temp	pH	SG	CR	bar	u	p	nu_p
05-06-91M	40	N/T	5.40	1.019	N/T	N/T	174	5	LOW
05-03-91F	40	N/T	5.40	1.009	89	HI	296	26	1389
				Mean:	141		1456	52	1709
				SD:	49		1661	32	769
				CV:	35.0		114	62.3	45
				Tests:	12		12	12	12

TABLE D

Date	Dose	Temp	pH	SG	CR	bar	u	p	nu_p
04-04-92S	130	95.0	5.80	1.013	196	0	4915	373	7728
03-28-92S	130	98.0	5.90	1.020	210	0	6565	287	5944
03-21-92S	110	95.0	5.50	1.021	216	0	9651	278	6580
03-14-92S	110	97.0	5.70	1.022	210	0	8964	282	6703
03-07-92S	110	96.0	6.30	1.014	186	0	4471	395	10880
03-02-92M	110	95.0	5.60	1.022	206	0	8778	254	6025
02-21-92F	120	96.0	6.20	1.016	181	0	5169	403	8970
02-15-92S	120	98.0	5.90	1.015	187	0	4525	306	6778
02-08-92S	120	96.0	6.10	1.017	181	0	5506	364	8074
01-31-92F	120	95.0	6.20	1.016	218	0	6896	425	11966
01-18-92S	120	96.0	5.50	1.021	224	0	9503	274	6031
01-11-92S	130	96.0	5.30	1.020	182	0	9494	249	5117
				Mean:	200	0	7036	324	7256
				SD:	16	0	2114	63	1467
				CV:	8.0	0	30	19.5	20.2
				Tests:	12	12	12	12	12

Case #3

Shown in Table E are examples of estimated plasma methadone levels for four patients demonstrating how to detect misuse of methadone.

TABLE E

Utilization of Plasma Methadone Levels
To Uncover Misuse of Methadone
Estimated Plasma Methadone Concentration (ng/ml), p

Sample	Patient A*	Patient B	Patient C***	Patient D
1	480	346	89	1247****
2	465	234	44	1173****
3	485	281	50	1061****
4	525	253	354	1343****
5	454	376	84	435
6	410	208	310	575
7	531	290	778	427
8	483	172**	8.00	514
9	403	0**	33	474

*Patient A ingests 90 mg/day of methadone q24 hr. as instructed. He ingests a dose in the clinic on Mon., Wed. and Fri., mean 24-hr. trough level is 470 ng/ml with a CV = 9.4%.

**Patient B receives 80 mg/day of methadone. She only gets a take home dose for Sunday. Expected mean value (samples 1–6) is 281 +/– 62 ng/ml. Sample 8 was taken 48 hr. after her last dose providing an estimate of plasma methadone half-life of about 65 hrs. Sample 9 is an example of substitution on a non-patient urine sample.

***Patient C ingests 50 mg/day in clinic on Mon., Wed. and Fri. Her expected plasma concentration should be about 170 ng/ml. She is likely diverting Tues, Thurs. and Sun. take home doses and spiking urines with exogenous methadone on other days. Solution was to withdraw take home doses.

****Patient D currently ingests 100 mg/day of methadone (samples 5–9). Previously, he was ingesting over 200 mg/day of methadone via supplementing with illicit methadone (samples 1–4). Solution was to slowly taper him back to 100 mg/day on a daily basis of clinic visits.

Cases #4 and #5

Shown in Tables F and G are data demonstrating how the statistical program is utilized by the computer to 'flag' a urine methadone value as being outside the acceptable range for the patient. With this data it is possible for a healthcare provider to speak with a patient about this abnormality before it becomes a continuing problem. Typically, lab errors are ruled out prior to discussion with the patient. Assuming no laboratory explanation is forthcoming, the healthcare provider can consider substitution of urine by the patient (often noted by variation in measured urinary parameters, including normalized creatine); ingestion of methadone on a non-24 hour basis; ingestion of additional and unapproved methadone; selling of take-home methadone doses; taking a medication interfering with the metabolism of methadone and so forth. Having an objective and quantitative methadone history to present to the patient overcomes the natural tendency for many patients to be untruthful.

TABLE F

Date	Dose	Temp	pH	SC	CR	u	p	nu_p	Pred
09-10-93F	140	95.0	7.11	1.013	307	3631	352	17072	High
09-08-93W	140	95.0	5.19	1.025	306	12847	204	4686	
09-02-93h	140	95.0	5.49	1.023	317	6345	154	3555	
08-30-93M	140	95.0	4.68	1.023	316	12629	144	3269	
08-26-93h	140	95.0	4.93	1.020	224	10227	186	4251	
08-23-93M	120	94.0	4.91	1.025	239	14105	172	4466	
08-20-93F	120	94.0	5.78	1.028	299	8194	172	4511	
08-17-93T	120	94.0	5.31	1.036	311	8814	145	3768	
08-13-93F	120	94.0	6.18	1.013	357	3161	314	8401	
08-10-93T	120	95.0	5.81	1.021	296	4634	173	4550	
08-06-93F	120	95.0	6.69	1.019	243	2923	252	6696	
08-03-93T	120	95.0	5.53	1.024	185	8645	201	5264	
				Mean:	283	8008	206	5130	
				SD:	49	3945	67	1710	
				CV:	17.3	49.2	32.4	33.3	
				Tests:	12	12	12	11	

TABLE G

Date	Dose	Temp	pH	SC	CR	u	p	nu_p	Pred
08-06-93F	130	96.0	4.88	1.025	491.	4305	97	1858	LOW
08-02-93M	130	96.0	4.81	1.024	215	13601	163	5922	
07-29-93h	130	96.0	5.05	1.019	211	11105	249	9089	
07-26-93M	130	95.0	LOW	1.014	214	8822	163	5865	
07-22-93h	130	96.0	4.52	1.028	421.	4431	98	1942	LOW
07-19-93M	130	95.0	4.66	1.021	258	25400	333	12050	
07-15-93h	130	96.0	5.96	1.003	LOW	5585	381	97615	HIGH
07-12-93m	130	96.0	4.76	1.021	228	14361	208	7550	
07-09-93F	130	94.0	4.76	1.015	230	10940	366	9563	
07-06-93T	130	96.0	5.20	1.024	249	17816	309	11313	
07-01-93h	130	96.0	5.10	1.012	224	6963	318	11630	
06-28-93M	130	97.0	LOW	1.011	241	7478	190	6841	
06-24-93h	130	N/T	LOW	1.009	232	6889	224	8088	
				Mean:	214	10585	231	8396	
				SD:	41	6037	89	3288	
				CV:	19.1	57	38.5	39.1	
				Tests:	12	13	13	13	

Case #6

Methadone concentration data were simultaneously measured using GC/MS and FPIA for urine obtained from five patients and plotted in FIG. 8 for comparison. Linear regression analysis shows that GCMS=0.97*FPIA=48, R=0.999: both methods are essentially equivalent. Similarly, methods other than GC/MS or FPIA could also be used, such as gas chromatography, high pressure liquid chromatography, chemical methods and so on, to sequentially follow raw urine methadone concentration patient data for utilization in this invention.

MEDICATION MAINTENANCE PROGRAMS

A patient is initially prescribed a medication and dose based on several factors. These ordinarily include the severity and duration of illness, amounts and types of medications previously used, current or previous physiological and/or physical dependence upon other prescription or illicit drugs, previous medical history, patient sex, pregnancy status, patient weight and ingestion of other therapeutic medications. Normally medication dose is adjusted upwardly until a patient no longer complains of residual signs and symptoms of his or her psychiatric and/or medical illness, is no longer experiencing withdrawal signs and symptoms if on a medication-replacement taper to abstinence program, or loses his or her desire to use illicit medications if a substance abuse problem exists. Medication dose is increased per published and accepted standard medical protocols for each family of psychiatric and medical drug, usually "x" mg every few days.

To determine compliance with the prescribed medication dose, random urine samples are obtained from the patient and analyzed in accordance with the invention as described in FIG. 9. If tested and determined to be unadulterated, a raw urine parent drug and/or its metabolites concentration is measured preferably using FPIA. Metabolites are those substances which result from the body's metabolism of the parent drug. The metabolites are detectable and part of the value obtained when measuring the raw urine medication concentration. The raw urine medication concentration (u) is next converted to a normalized urine medication concentration (nu) as discussed below. Over time, a normalized urine medication concentration-daily medication dose relationship is derived for each individual patient, which can be compared to the relationship expected for that particular patient. Alternatively, by adjusting the normalized urine medication concentration relative to the urinary pharmacokinetic parameters for each medication, a urinary-parameter normalized urine medication concentration (nu_p) may be calculated and compared to that expected for an average patient to determine compliance with the patient's prescribe medication dose.

Again, if the relationships between the present nu and the expected nu are not similar, either the patient's metabolism

rate is causing an over- or under-effectiveness of the prescribed dose or the patient is not complying with his or her prescribed dose. If related to the patient's individual metabolism rate, a physician can now optimize the patient's medication dose to achieve an efficacious and safe plasma medication concentration. Once the optimum medication dose is established for the patient, a physician can monitor the patient for compliance with his or her prescribed dose by comparing either the nu or the nu_μ with their expected values for the particular medication dose; hence, uncovering covert medication diversion or supplementing.

The steps of testing for adultration of the urine sample and determination of the raw urine medication concentration are also utilized in determining compliance with a medication maintanence program and follow the same procedures as discussed above in methadone maintanence programs.

Determination of Normalized Urine Medication Concentration

The normalized urine medication concentration, nu, is statistically constant for each patient relative to the medication dose regardless of an individual's medication metabolism (if the immunoreactivity for the FPIA antibody is nonselective between parent and drug metabolites) and daily changes in urine parameters. In determining how to calculate nu, the linear relationship developed above between the urine volume production rate factor (UVPRF) and the reverse urine creatinine excretion factor (RUCEF) was utilized. This relationship, as shown in FIG. 4, is represented as follows:

$$RUCEF=0.942(SE\ 0.013)\cdot UVPRF+0.121(SE\ 0.043) \quad (13)$$

$$u'/u=0.942\cdot v/v'+0.121 \quad (14)$$

Therefore, contrary to the traditional teachings of those skilled in the art, urine drug and metabolite concentrations, u, are inversely related to the volume, v, of urine produced by the kidneys.

Following the same logic in determining plasma methadone concentration equation, the standard dimensionally correct renal clearance equation is utilized, which is

$$cl=(u\cdot v)/t \quad (15)$$

Assuming that at steady-state plasma medication concentration and renal clearance are constant, the product (u·v) must also be constant at any particular time point. It follows that an empirical mathematical relationship exists between u and v such that given an arbitrary urine volume production rate v' and an equivalent u' at a reference point (specific gravity 1.030):

$$\{u\cdot v\}_{\text{SG actual}}=\{u'\cdot v'\}_{\text{SG }1.030} \quad (16)$$

or upon rearrangement for u' gives,

$$u'=u\cdot(v/v') \quad (17)$$

where the products given in Equations (16) and (17) are those measured for a spot urine collected with an actual specific gravity (u,v) and a corrected specific gravity typical of a morning void of 1.030 (u',v'). Utilizing the linear relationship that exists between urine volume production rate factor (UVPRF) and the specific gravity factor (SGF) in Equation (10) and combining it with Equation (17), a normalized urine medication concentrations can be calculated as follows:

$$nu=u'=u\cdot(v/v')=u\cdot UVPRF=u\cdot(k_1\cdot SGF-k_2) \quad (18)$$

wherein k_1 is a constant equal to 2.43 and k_2 is a constant equal to 1.43.

Determination of Urinary-Parameter Normalized Urine Concentration

The parameters of a patient's urine vary from one day to the next dependant upon the type and quantities of foods and beverages ingested. Additionally, individuals metabolize these substances, as well as medication, at different rates. By adjusting the normalized urine medication concentration to account for these variations, the urinary-parameter normalized urine medication concentration (nu_μ) is calculated. Use of the nu_μ is preferable in the clinical setting because nu_μ is an alteration based on pharmacokinetic parameters important for a particular drug or family of drugs, thus providing a value that may be compared to that expected of the average patient.

Some important pharmacokinetic parameters include: patient body weight, whether a drug is a weak acid or weak base, how a drug is absorbed into tissues and blood, how the drug is administered (ie., orally, intravenously), whether a drug is a controlled release formulation, how a drug distributes in the body (patient volume of distribution, protein binding, tissue binding, lipidicity, redistribution), whether biotransformation occurs (cross-reactive metabolites, chemical half-life, tissue half-life), how the drug is excreted (renal clearance, hepatic clearance, tissue clearance, fecal clearance, dosing rate and amount, final steady-state concentrations of peak and trough levels of drug, zero order, first order or mixed order biotransformation reaction). These parameters may be measured by utilizing readily available values such as patient body weight, prescribed medication dose, urine pH, and urine volume production rate. For example, pH is an important variable if one is monitoring weak bases such as methadone, but is of only minor importance when monitoring weak acids such as the glucuronide derivatives of benzodiazepines and opioids. The pharmacokinetic parameters for each drug are available in medical references such as Goodman & Gillman, *The Pharmacological Basis of Therapeutics*, 8th Edition, Pergamon Press, 1990.

The relationships for any medication family between nu and the medication pharmacokinetic parameters are empirically developed using regression analysis. For example, in the case of diazepam and alprazolam, urine pH is not important. However, the following equation linearly adjusts each patient value to a standard weight of 70 kg (154 lb) for useful results:

$$nu_\mu(\text{patient body weight}/k_3)\cdot u\cdot UVPRF \quad (19)$$

wherein k_3 is a constant equal to 70. This value, once accurately established for a patient within a statistical margin of error, is used to evaluate medication diversion or supplementation in the patient by comparing subsequent calculations of this value with that an expected value of the average patient. If the subsequent calculation is similar to the expected value, the patient is complying with his prescribed dose.

Statistical methods similar to those proposed for methadone can be used to establish confidence limits.

Determining Daily Medication Dose Ingested

Once the urinary-parameter normalized urine medication concentration is calculated from Equation (19), it and the patient's daily medication dose are compared to that

expected from a standard population. FIGS. 10 and 11 show how urinary-parameter normalized urine medication concentration varies with dose for patients prescribed and properly ingesting diazepam and alprazolam. Using these graphs, a clinician can estimate how a change of dose will effect the patient's urine medication concentration. If a patient's urinary-parameter normalized urine medication concentration is less than that expected from FIGS. 10 or 11, such a result may indicate that the patient is diverting the medication to others or simply not using it. Higher concentrations per dose suggest the opposite of the above.

A further appreciation for consistency of medication ingestion by patients is shown in FIG. 12. The mean alprazolam normalized concentrations and standard deviations for several patients are plotted. As is apparent, all patients except one had SD of about +/−15% of the mean. The lone patient with a much higher variation was found to be ingesting on average 4 mg alprazolam per day, ranging from 2 to 8 mg per day.

In general, it has been determined that most patients ingesting proper, prescribed dosages of medications produce a point-of-time, spot nu_p value that is often within +/−20% of their individual mean value for any particular medication and dose. Although, actual acceptance values must be determined for each medication and assay method.

Two methods of interpreting urine medication results for compliance monitoring have now been developed. The first and most primitive method is to simply establish, using data from controls and compliant patients, mean drug levels and the expected ranges (minimums and maximums) for the nu_p of each particular medication at each particular daily, total dose amount. For example, it has been determined that the following equations for estimating the expected mean medication concentrations as a function of total, daily medication dose are useful for monitoring the benzodiazepine parent drugs and metabolites using FPIA (temazepam, clonidine, flurazepam and oxazepam are similar to diazepam):

$$\text{Alprazolam: } nu_p = 910(\text{SE } 31.4) * \text{Dose, SEE } 210 \quad (20)$$

$$\text{Diazepam: } nu_p = 267(\text{SE } 16.9) * \text{Dose, SEE } 806 \quad (21)$$

Acceptable maximum and minimum ranges of the nu_p calculated by Equation (19) for any patient (after ruling out metabolic problems) are simply given as +/−20% of the expected mean value of nu_p at any dose for a compliant patient as calculated by Equation (20) or (21).

A second and more sophisticated method for evaluating individual normalized medication concentrations for a spot urine sample utilizes probability theory and prediction intervals. To use this method, one calculates mean and SD for each control and patient sample set and plots the SD for each subject versus size of each subject's sample set. Using standard prediction formulas and confidence limits on the population of SD, one estimates from the actual data (each drug and drug family is unique) the true standard deviation for the population of all persons ingesting the drug properly. Given this value for the true population SD, other prediction equations can be derived of the form, acceptable value= patient mean +/−x·SD, where x is a factor whose value is dependent upon sample size and desired confidence limit, eg, 95, 97.5, 99, and 99.999%. Once these values have been determined, the urinary-parameter normalized urine concentration calculated by Equation (19) can be compared to an expected range and noted as low, acceptable or high.

Given sufficient control and patient data and a method of analysis, preferably though not limited to quantitative immunoassay like FPIA, similar relationships for mean urinary-parameter normalized urine medication concentrations as a functions of daily medication dose can easily be derived both for other drugs in the benzodiazepine family and for other distinctly different chemical families, making this method broadly useful. Therefore, this method is useful not only for determining the average amounts of medication taken each day, but how irregular the patient may be from one day to another.

Clinical Examples

Case #6

J. W. is a 34 year old male presented for treatment of an anxiety disorder. He had been ingesting 1.5 mg alprazolam daily. After placing the patient into an individualized, anxiety-reduction therapy program, his psychiatrist was able to gradually decrease his alprazolam to abstinence. The patient later attended college without evidence of return to medication use. Shown in Table H is a partial representation of a standard computer printout for this compliant patient who was slowly tapered from alprazolam using the nu_p method as an aid to downward dose adjustments. The last column in the figure marked BENZ represents nu_p values for the patient which are quite constant once specific gravity and patient weight corrections are made to the raw urine medication concentration (u).

TABLE H

Date	Temp	pH	SG	CR	nu_p Ben
09-28-92M	98.0	5.40	1.024	253	280
09-22-92T	98.0	5.70	1.028	235	182
09-21-92M	96.0	5.10	1.025	279	228
09-17-92h	96.0	5.60	1.029	248	168
09-16-92W	98.0	5.30	1.028	1991.	168
08-27-92h	98.0	5.40	1.025	234	184
08-24-92M	98.0	5.50	1.029	289	162
			Mean:	257	196
			SD:	48	44
			CV:	9.6	21.9
			Tests:	12	7
08-14-92F	97.0	5.40	1.027	271	260
08-10-92M	97.0	5.40	1.029	260	388
08-06-92h	98.0	5.30	1.028	242	352
08-05-92W	98.0	5.80	1.029	234	306
07-29-92W	97.0	5.40	1.028	2021.	252
07-27-92M	96.0	5.30	1.024	271	420
07-24-92F	98.0	5.70	1.024	244	522
07-20-92M	98.0	7.20	1.022	315	662
07-17-92F	97.0	6.60	1.029	219	426
07-15-92W	97.0	5.90	1.021	271	654
			Mean:	254	422
			SD:	28	144
			CV:	11.1	34.1
			Tests:	12	10
06-01-92M	97.0	5.80	1.030	286	718
05-27-92W	97.0	5.40	1.013	267	1032
05-26-92T	94.0	5.60	1.030	283	720
05-21-92h	98.0	6.00	1.021	286	830
05-19-92T	96.0	5.70	1.023	278	948
05-13-92W	98.0	5.60	1.029	241	670
05-09-92S	96.0	6.40	1.023	269	784
05-05-92T	96.0	5.50	1.018	284	1098
05-04-92M	98.0	5.70	1.027	256	840
04-30-92h	95.0	5.80	HI	277	940
04-27-92M	96.0	5.40	1.011	288	1200
04-24-92F	96.0	5.50	HI	277	826
			Mean:	274	884
			SD:	14	164

TABLE H-continued

Date	Temp	pH	SG	CR	nu_p Ben
			CV:	5.1	18.4
			Tests:	12	12
04-30-92M	98.0	5.40	1.022	335	1164
04-15-92W	96.0	5.70	1.024	268	1014
04-13-92M	96.0	5.90	1.019	271	1174
04-10-92F	98.0	5.70	1.021	377H	1246
04-06-92M	98.0	5.90	1.028	261	858
04-02 92h	96.0	5.70	1.025	271	1052
03-30-92M	94.0	5.60	1.021	303	1512
03-25-92W	98.0	5.30	1.021	271	1346
03-24-92T	98.0	6.00	1.023	243	1330
03-20-92F	96.0	5.80	1.024	272	1278
03-16-92M	94.0	5.50	1.022	286	1464
03-13-92F	96.0	5.70	1.019	277	1710
			Mean:	285	1262
			SD:	32	234
			CV:	11.2	18.5
			Tests:	12	12

Case #7

R. C. is a 38 year old long-term opiate addict who was prescribed alprazolam by an outside psychiatrist. This patient's drug use was monitored to insure that he was compliant with his prescription. Data for this patient is shown in FIG. 12 and Table I. Table I is the urine data sheet demonstrating large variation in the BENZ levels consistent with irregular ingestion of alprazolam. FIG. 12 shows the elevated SD measured for this non-compliant patient as compared to others.

TABLE I

Date	Dose	pH	SG	Ben
04-05-90	0	5.0	1.016	2896**
04-13-90	80	5.5	1.018	6128**
04-16-90	80	8.0	1.005	6252**
04-23-90	80	5.5	1.010	3358**
04-30-90	80	5.5	1.000	4110**
05-18-90	90	5.5	1.008	3322**
06-01-90	90	5.5	1.013	1512**
06-04-90	90	5.1	1.015	1790**
06-11-90	90	5.0	1.001	2468**
06-18-90	90	5.6	1.006	1836**
06-29-90	90	5.0	1.005	2664**
07-13-90	90	6.1	1.016	684**
07-16-90	90	5.5	1.001	0
07-27-90	90	5.1	1.006	3123**
07-30-90	90	5.0	1.005	2932**
08-06-90	90	5.5	1.015	2928**
08-15-90	90	7.1	1.009	2648**
08-20-90	90	5.0	1.018	2502**
08-29-90	90	5.6	1.016	2860**
09-04-90	90	6.5	1.025	HI**
09-05-90	90	6.1	1.019	3468**
09-10 90	90	5.0	1.013	4194**
09-24-90	90	7.0	1.005	4962**
10-01-90	90	5.0	1.010	6552**
10-02-90	90	6.1	1.010	2816**
10-08-90	90	5.1	1.023	2510**

***Xmax level: mean = 4268 ng/ml, CV = 49.8% (normalized to 70 kg)

Case #8

A. S. is a 42 year old female requiring treatment of severe, episodic pain associated with spasm of the levator ani muscle of the pelvic floor. She was prescribed Tylenol #3 (30 mg of codeine) po q8h for relief of severe pain, prescribed Norflex 100 mg po bid to help relieve referred spasms of the buttock area and entered into a Rolfing program to realign her axial skeleton and balance the pelvic musculature. Following the above treatment plan her problem resolved over a 6 month period allowing discontinuation of all medications other than occasional Norflex.

Shown in FIG. 13 are mean nu_p values for codeine as a function of daily, total dose. Although the numbers are different, results are qualitatively similar to those seen with the benzodiazepines and methadone. Her mean codeine level while stabilized on 90 mg of codeine qd, as shown on FIG. 13, should be 19,102 +/−3840 ng/ml. A summary of her weekly urine test results are also shown in Table J.

TABLE J

Date	Dose	Temp	pH	SG	CR	Coc	Opi
09-10-93F	9-0	94.0	LOW	1.013	42L		20471
09-03-93F	9-0	95.0	5.60	1.017	343		15492
08-27-93F	9-0	94.0	5.62	1.014	292		18659
08-18-93W	9-0	96.0	5.50	1.022	355	0	21775
08-03-93T	9-0	92.0	4.72	1.010	372		13830
07-30-92F	9-0	94.0	5.53	1.023	390		20457
07-16-93F	9-0	N/T	5.83	1.015	347	0	25039
06-28-93M	9-0	96.0	6.10	1.017	383		21894
06-18-93F	9-0	95.0	5.90	1.019	368		14257
				Mean:	349		19102
				SD:	34		3840
				CV:	9.5		20.1
				Tests	9		9

Case #9

W. K. is a 44 year old male requiring opioid medications for severe arachnoiditis following surgery in the lumber spine. He was prescribed oxycodone without acetaminophen since he is status post removal of one kidney because of renal carcinoma. Shown in Table K are his oxycodone levels (40 mg per day total dose) which are within acceptable limits of 800–1600 ng/ml.

TABLE K

Date	Temp	pH	SG	CR	nu_p Opi
02-14-94M	98.0	5.25	1.010	446H	1536 Rx
02-10-94h	96.0	5.11	1.024	302	791 Rx
02-07-94M	94.0	5.20	1.015	359	1154 Rx
02-03-94h	96.0	5.33	1.011	186L	1062 Rx
01-31-94M	N/T	7.13	1.017	299	928 Rx
01-27-94h	N/T	5.23	1.013	286	583 Rx
01-24-94M	N/T	5.41	1.011	264	1505 Rx
01-20-94h	N/T	5.59	1.011	263	937 Rx
01-17-94M	94.0	5.76	1.010	447H	1252 Rx
01-13-94h	95.0	5.51	1.009	309	1562 Rx
01-10-94M	94.0	5.44	1.012	415	1605 Rx
01-06-94h	94.0	6.12	1.004	223	1760 Rx
			Mean:	324	1206
			SD:	79	362
			CV:	24.4	30.0
			Tests:	12	12

It is thus seen that methods are now provided that monitor patients who have been placed on medication maintenance programs for compliance without the need to draw blood. The invention utilizes readily obtainable urine medication concentrations from evaluation of patient urine samples by FPIA to determine normalized and urinary-parameter urine medication concentration, which can be respectively compared to historical patient data and general population data

to confirm prescription compliance. Plasma medication concentrations may also be determined. The methods are clinically practical without high laboratory testing cost, the invasiveness of withdrawing blood, and the added exposure to medical professionals of patient blood having high probability of hepatitis and HIV infection.

While this invention has been described in detail with particular reference to preferred methods thereof, it should be understood that many modifications, additions and deletions may be made thereto without departure from the spirit and scope of the invention, including application to other drugs and medications, as set forth in the following claims.

I claim:

1. A method of monitoring compliance of a patient that has been placed on a medication maintenance program with a prescribed medication dosage, and with the method comprising the steps of

(a) obtaining a sample of the patient's urine,

(b) measuring the concentration of the medication or its metabolites in the urine and the urine specific gravity,

(c) calculating a normalized urine medication concentration as the product of the measured medication concentration in the urine and a specific gravity factor, the specific gravity factor being a ratio of specific gravity of a typical morning void for the general population to the patient measured urine specific gravity, and

(d) comparing the normalized urine medication concentration with an expected medication concentration value for the patient for the maintenance program prescribed to determine any significant differences therebetween as an indication of noncompliance.

2. The method of claim 1 wherein the specific gravity of a typical morning void for the general population has a value of 1.030.

3. A method of monitoring compliance of a patient that has been placed on a medication maintenance program with a prescribed medication dosage, and with the method comprising the steps of

(a) obtaining a sample of the patient's urine,

(b) measuring the concentration of the medication in the urine, the urine specific gravity and at least one selected pharmacokinetic parameter of the medication,

(c) calculating a urinary-parameter normalized urine medication concentration as the product of the measured medication concentration in the urine, a specific gravity factor and the at least one selected pharmacokinetic parameter, the specific gravity factor being a ratio of specific gravity of a typical morning void for the general population to the patient measured urine specific gravity, and

(d) comparing the urinary-parameter normalized urine medication concentration with an expected medication concentration value for an average compliant patient for the maintenance program prescribed to determine any significant differences therebetween as an indication of noncompliance.

4. The method of claim 3 wherein the specific gravity of a typical morning void for the general population has a value of 1.030.

5. A method of monitoring compliance of a patient that has been placed on a methadone maintenance program in accordance with claim 3 and wherein step (b) the concentration of methadone is measured.

6. The method of claim 5 wherein step (b) methadone dose, patient body weight and urine pH are measured as the selected pharmacokinetic parameters.

7. A method of monitoring compliance of a patient that has been placed on a methadone maintenance program which comprises the steps of

(a) obtaining a sample of the patient's urine,

(b) measuring the concentration of methadone, the specific gravity and the pH value of the urine sample,

(c) calculating the concentration of methadone of the plasma as the product of the measured concentration of methadone of the urine, a specific gravity factor and urine pH, the specific gravity factor being a ratio of specific gravity of a typical morning void for the general population to the patient measured urine specific gravity, and

(d) comparing the calculated concentration of methadone of the plasma with an expected value for the maintenance program prescribed.

8. The method of claim 7 wherein the specific gravity of a typical morning void for the general population has a value of 1.030.

* * * * *

EXHIBIT B

US006124136A

United States Patent [19]

Kell

[11] Patent Number: 6,124,136

[45] Date of Patent: Sep. 26, 2000

[54] METHOD OF MONITORING COMPLIANCE WITH METHADONE TREATMENT PROGRAM

[75] Inventor: Michael Kell, Atlanta, Ga.

[73] Assignee: U. D. Testing, Inc., Gainesville, Ga.

[21] Appl. No.: 08/145,821

[22] Filed: Nov. 2, 1993

[51] Int. Cl.[7] G01N 33/48

[52] U.S. Cl. 436/111; 436/816; 436/901

[58] Field of Search 436/111, 816, 436/901; 422/61

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Primary Examiner—Lyle A. Alexander

Attorney, Agent, or Firm—Kennedy, Davis & Hodge LLP

[57] ABSTRACT

A method of monitoring compliance of a patient that has been placed on a methadone maintenance program by determining plasma methadone concentration from urine methadone concentration. An unadulterated urine sample is obtained from the patient. The urine methadone concentration, pH, and specific gravity are measured. The plasma methadone concentration is calculated as a function of urine methadone concentration, specific gravity, and pH. The calculated plasma methadone concentration is compared with an expected value for the maintenance program prescribed.

16 Claims, 5 Drawing Sheets

FIG 1

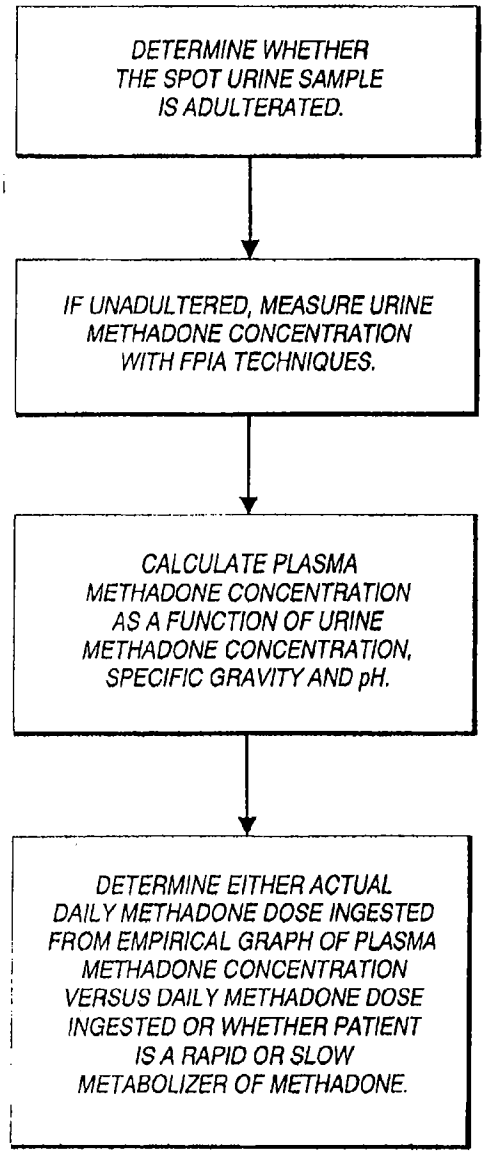
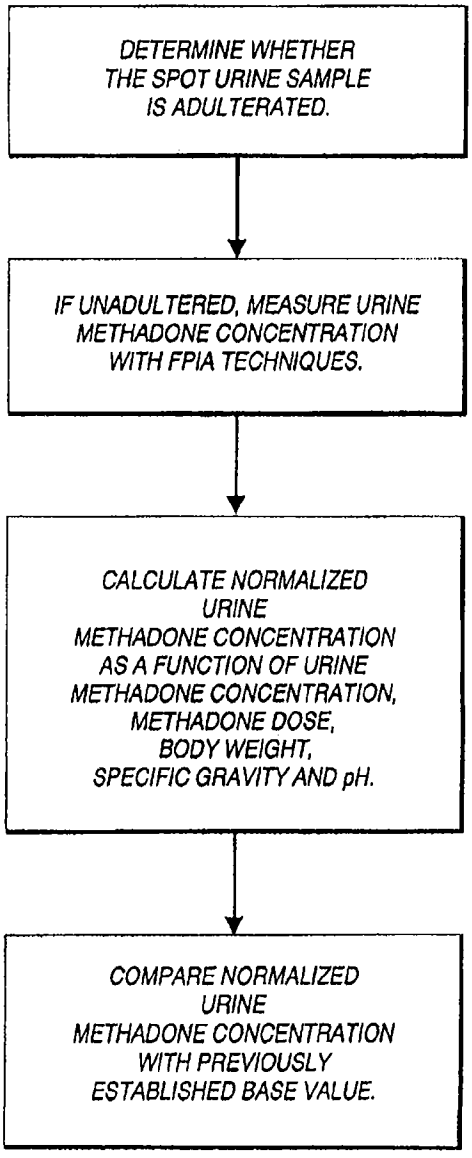

DETERMINE WHETHER THE SPOT URINE SAMPLE IS ADULTERATED.
IF UNADULTERED, MEASURE URINE METHADONE CONCENTRATION WITH FPIA TECHNIQUES.
CALCULATE PLASMA METHADONE CONCENTRATION AS A FUNCTION OF URINE METHADONE CONCENTRATION, SPECIFIC GRAVITY AND pH.
DETERMINE EITHER ACTUAL DAILY METHADONE DOSE INGESTED FROM EMPIRICAL GRAPH OF PLASMA METHADONE CONCENTRATION VERSUS DAILY METHADONE DOSE INGESTED OR WHETHER PATIENT IS A RAPID OR SLOW METABOLIZER OF METHADONE.

FIG 2


DETERMINE WHETHER THE SPOT URINE SAMPLE IS ADULTERATED.
IF UNADULTERED, MEASURE URINE METHADONE CONCENTRATION WITH FPIA TECHNIQUES.
CALCULATE NORMALIZED URINE METHADONE CONCENTRATION AS A FUNCTION OF URINE METHADONE CONCENTRATION, METHADONE DOSE, BODY WEIGHT, SPECIFIC GRAVITY AND pH.
COMPARE NORMALIZED URINE METHADONE CONCENTRATION WITH PREVIOUSLY ESTABLISHED BASE VALUE.

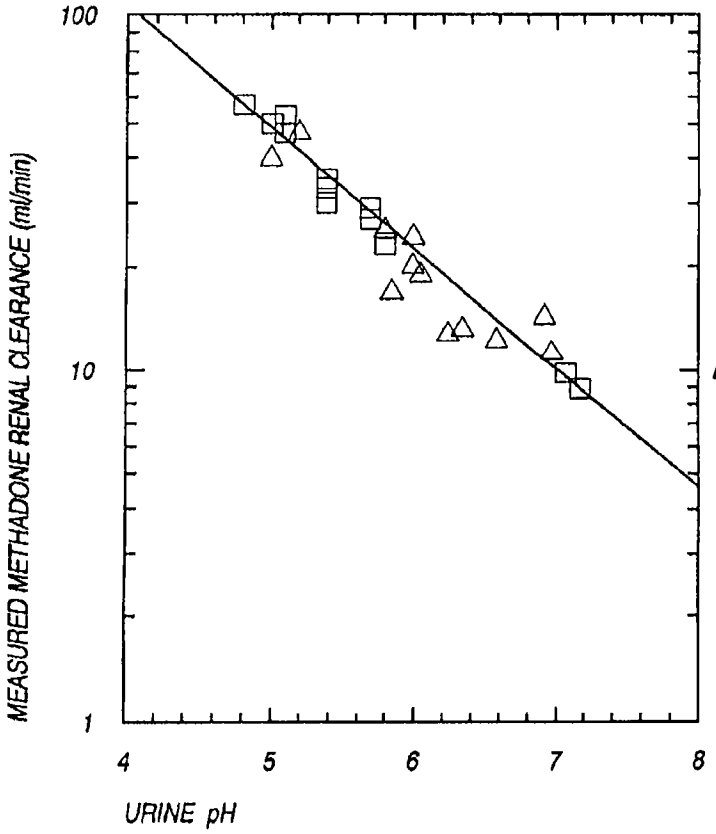

100
10
1
MEASURED METHADONE RENAL CLEARANCE (ml/min)
4
5
6
7
8
URINE pH

FIG 3

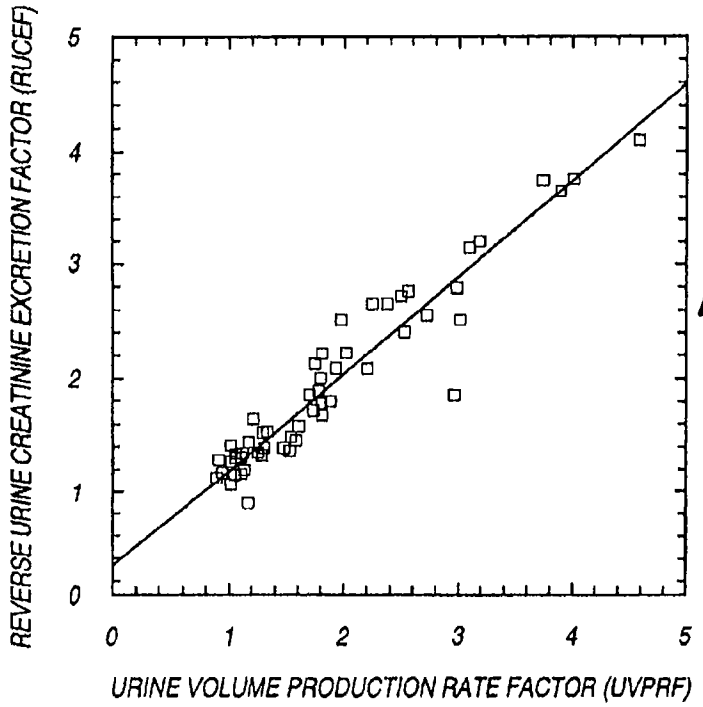

5
4
3
2
1
0
REVERSE URINE CREATININE EXCRETION FACTOR (RUCEF)
0
1
2
3
4
5
URINE VOLUME PRODUCTION RATE FACTOR (UVPRF)

FIG 4

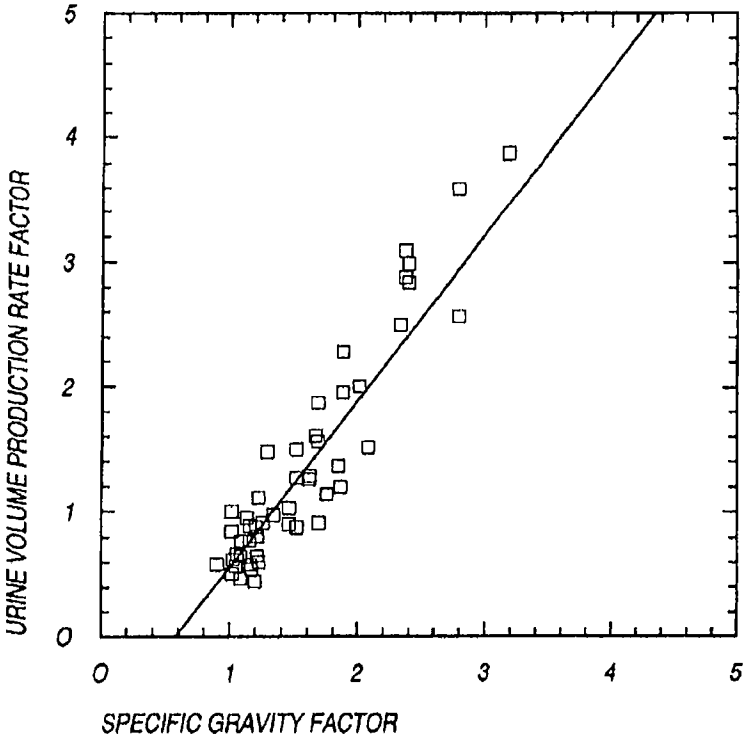

URINE VOLUME PRODUCTION RATE FACTOR
SPECIFIC GRAVITY FACTOR
0
1
2
3
4
5

FIG 5

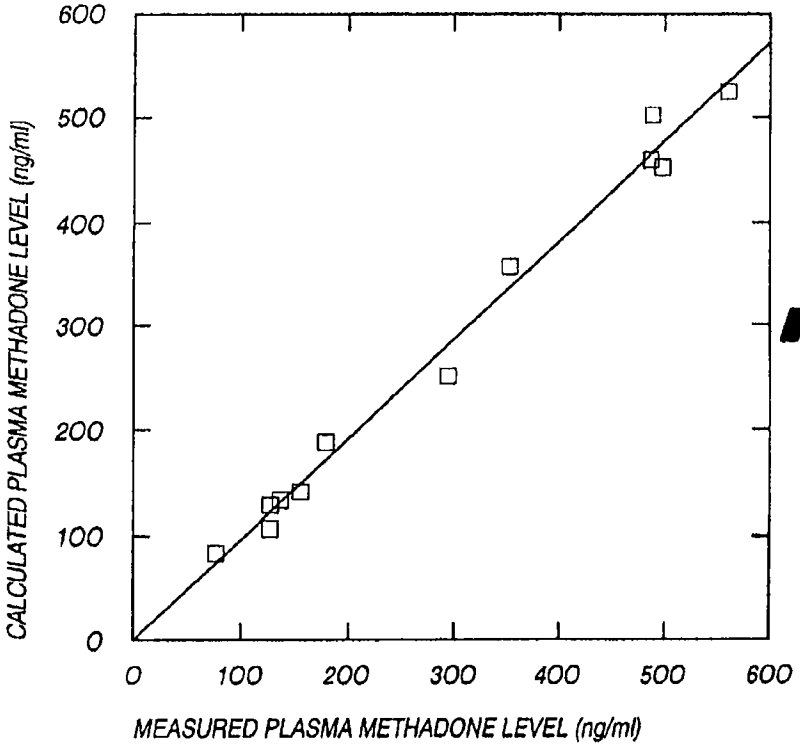

CALCULATED PLASMA METHADONE LEVEL (ng/ml)
MEASURED PLASMA METHADONE LEVEL (ng/ml)
0
100
200
300
400
500
600

FIG 7

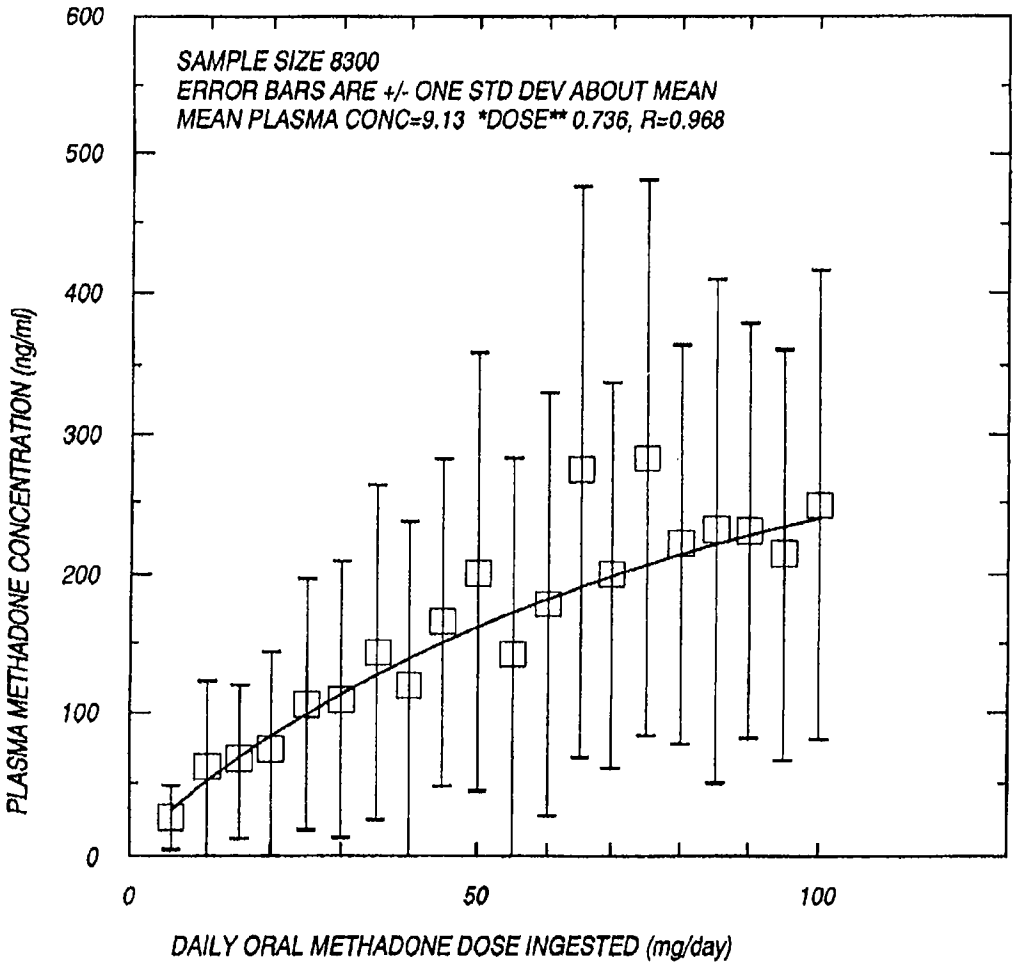

SAMPLE SIZE 8300
ERROR BARS ARE +/- ONE STD DEV ABOUT MEAN
MEAN PLASMA CONC=9.13 *DOSE** 0.736, R=0.968
PLASMA METHADONE CONCENTRATION (ng/ml)
600
500
400
300
200
100
0
0
50
100
DAILY ORAL METHADONE DOSE INGESTED (mg/day)

FIG 6

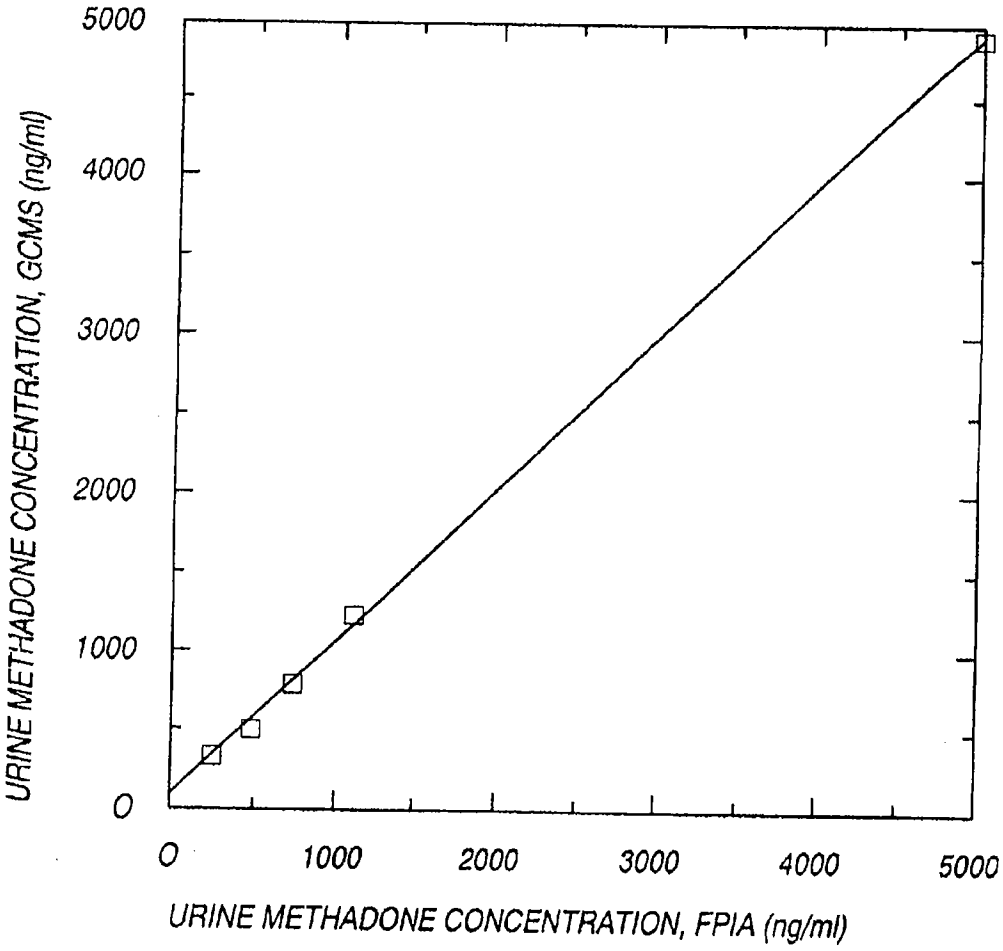

5000
4000
3000
2000
1000
0
URINE METHADONE CONCENTRATION, GCMS (ng/ml)
0
1000
2000
3000
4000
5000
URINE METHADONE CONCENTRATION, FPIA (ng/ml)

FIG 8

METHOD OF MONITORING COMPLIANCE WITH METHADONE TREATMENT PROGRAM

TECHNICAL FIELD

The present invention relates to therapeutic drug monitoring. More particularly, the invention relates to methods of monitoring the amounts of methadone ingested and resultant concentration levels in specific bio-fluids in patients placed on methadone treatment programs for compliance therewith either for treatment of a biochemical dependence upon opioid drugs and/or alleviation of suffering from opioid-responsive, chronic pain syndromes.

BACKGROUND OF THE INVENTION

Opioids are a class of alkaloids comprised of natural analogs, chemically-modified natural analogs and synthetic congeners which are biologically similar in action to endogenously produced mammalian neurohormones, the enkephalins and the endorphins; which are important for mood regulation, biochemical homeostasis and relief of pain. Opioids generally function by inhibiting or modifying nociceptive transmissions into and within the spinal cord and higher central nervous system, including the limbic structures of the brain; hence, alleviating pain and maintaining normal mood. Secondary effects, which generally are undesirable, but to which tolerance develops with continued use, consist of sedation, respiratory depression and euphoria.

Opioid alkaloids, be they natural analogs or synthetic congeners, are highly addictive compounds, that with repetitive use, can damage and permanently interfere with the proper functioning of an organism's neural, hormonal, immunological and biochemical processes. Opioids are generally derived from the opium poppy, Papaver somniferum, or are synthetically manufactured. Common opioids include: codeine, propoxyphene, meperidine, heroin, morphine, oxycodone, hydromorphone, hydrocodone and paregoric.

A majority of persons who become biochemically dependent upon opioids either through prescription or illegal use experience great difficulty eliminating their dependency upon such drugs. When independent efforts fail and abuse continues, an opioid or narcotics addict may enter into an extended rehabilitative treatment program designed to prevent continued drug use and the associated negative medical and social consequences; with methadone maintenance programs now being the most commonly employed and potentially the most efficacious treatment modality. Such patients are treated under specific requirements of the Federal Register 21 CFR Part 291, attending a clinic for observed ingestion of methadone once, twice, thrice or more times a week.

Another important and generally accepted use for methadone within the medical community is alleviation of severe, organically-based pain syndromes in persons with cancer, nerve injuries, musculoskeletal damage and so on.

Methadone is a synthetic opioid which: (1) prevents the occurrence of withdrawal symptoms and drug cravings that occur when use of other opioids is discontinued, (2) prevents euphoria and drug reward when other opioids are ingested, inhaled or injected and (3) alleviates nociceptive and neuropathic sensory input into the central nervous system by its actions as a potent, and nearly pure (no interfering metabolites), agonist for the mu-receptor subfamily of the larger family of opioid cell membrane binding/transduction sites. Moreover, methadone when given in properly prescribed doses, unlike other potent and short half-life opioids, has not been shown to cause permanent and detrimental changes in a patient's biochemistry; making it safe to prescribe for extended time frames.

Typically, both in standard methadone maintenance programs and in chronic pain clinics utilizing methadone, physicians combine psychotherapy, psychosocial counseling, medical care and qualitative urine drug screening with prescribed daily doses of methadone to reduce illicit (illegal and/or not medically approved) opioid use.

Although illicit opioid use tends to decrease as methadone dose increases, a significant percentage of patients continue to abuse opioids even though apparently maintained on high methadone doses. Continued use of opioids by these patients may be attributed to several factors: (1) poor bioavailability and/or rapid hepatic metabolism of methadone resulting in plasma and blood methadone levels too low for alleviating the signs and symptoms of opioid withdrawal, blocking the euphorogenic effects of other opioids and normalizing mood, (2) diversion of methadone by patients not attending a clinic every day to illicit use by other addicts and (3) ingestion of non-opioid drugs such as barbiturates and anticonvulsants that counter the effect of methadone.

Monitoring of patients in methadone maintenance programs, including those dealing with chronic pain patients, aids physicians in effectively adjusting the prescribed methadone dose and in assuring patient compliance with their prescribed dose and medical treatment. Current methods commonly utilized for monitoring patients enrolled in methadone maintenance treatment programs are clinical observation for opioid intoxication or withdrawal; and less frequently, scheduled or random, repetitive, qualitative urine drug screening for uncovering illicit opioid use and insuring that methadone is indeed contained within the urine sample. Occasionally, research centers may directly measure a patient's plasma methadone concentration by obtaining a blood sample from the patient.

Clinical observation involves individual counseling and close personal supervision by physicians for evaluating the effects of a patient's methadone dose and observing signs of opioid intoxication or withdrawal. Physicians observe physiological signs and symptoms, listen to patient complaints and degree of pain relief, and evaluate psychological changes over time. This method is time consuming, expensive and highly subjective.

To supplement clinical evaluations, physicians also commonly monitor suspected illicit opioid use and ingestion of methadone by qualitatively analyzing urine for opioid-like and methadone-like immunoreactivity. A standard laboratory procedure used for this is enzyme-multiplied immunoassay technique or EMIT. Utilizing an arbitrary cutoff value, this method provides the clinician with only a simple positive or negative indication of the possible presence or absence of opioids and methadone in a patient's urine. It does not provide information concerning the time or amount of last drug use or whether or not the prescribed dose of methadone was ingested properly, diverted or supplemented.

Currently, utilizing only clinical evaluation and/or qualitative urine drug screening test results, physicians attempt to assess the condition of each patient and adjust methadone dose accordingly. For example, if a patient is continually testing positive for opioids or complains of continuing subjective opioid withdrawal symptoms, a physician may conclude that the currently prescribed dose of methadone is not sufficient to curb the body's desire for opioids and may increase the prescribed dosage. This highly subjective monitoring method can result in over-medication, patients being

given more methadone than they require, creating an unnecessary reliance on methadone. Alternately, physicians sometimes conclude, erroneously, that a patient's methadone dose should be sufficient to prevent opioid withdrawal and drug cravings and deny the patient a further increase sufficient to stop illicit opioid use. Such action can expose the patient to further intravenous drug use and the associated negative medical and social consequences which can follow—HIV, hepatitis, blood poisoning and so on.

To eliminate illicit opioid use, analytical studies using venous blood samples obtained from stable patients have shown that plasma methadone concentrations ranging from 150–600 ng/ml are necessary. Unfortunately, measurement of plasma methadone concentration requires the use of time consuming, expensive, and highly technical analytical procedures such as high pressure liquid chromatography and gas chromatograph/mass spectrometry. Additionally, for many patients obtaining plasma samples is invasive, offensive and difficult due to inadequate venous access. Medical professionals must also be concerned about their own health safety in doing this since they are exposed to blood products from a patient group with high prevalence to hepatitis and HIV infection. Therefore, such procedures are conducted only in research centers and are not generally utilized in standard methadone maintenance programs.

The methods described above, while providing some useful information relative to patient opioid use and treatment compliance, have distinct drawbacks which limit their usefulness in daily application for methadone maintenance programs. Therefore, it is seen that a need remains for a better method of monitoring opioid addicted patients who have been placed on methadone maintenance programs for compliance therewith. It is to the provision of such that the present invention is primarily directed.

SUMMARY OF THE INVENTION

In accordance with the present invention, a patient's urine, rather than blood or plasma, is analyzed for methadone concentration as an indicator of plasma methadone concentration which in turn provides a correlation to methadone dose ingested. This information may be used to monitor the patient's compliance with a prescribed methadone program. It also can be used to establish the proper methadone dose.

A patient is initially prescribed a methadone dose based on several factors including the severity and duration of opioid addiction, amount of opioid previously used, dependence upon other non-opioid drugs, previous medical history, patient sex, pregnancy status, patient weight and ingestion of other therapeutic medications. Normally methadone dose is adjusted upwardly until a patient no longer complains of withdrawal signs and symptoms and loses his or her desire to use illicit opioids. Generally, attaining 24-hour trough plasma methadone concentrations between 150–600 ng/ml , which are generally recognized in past studies as most effective in deterring illicit opioid use, are desirable.

As methadone dose is increased, usually 10–20 mg every few days, the patient's 24-hour trough plasma methadone concentration, as calculated by the present invention, is compared to previously measured plasma methadone concentrations; helping the physician determine both how the patient is metabolizing methadone and what the most likely final methadone dose will be. Over time, a unique plasma concentration-daily methadone dose relationship is derived for each individual patient, which can be compared to the relationship expected for that particular patient or for an average patient. If the two relationships are not similar, the patient's metabolism rate may account for any over- or under-effectiveness of the prescribed dose. A physician, in accounting for the patient's individual metabolism rate, can now optimize the patient's methadone dose to achieve an efficacious and safe plasma methadone concentration. Further, once the optimum methadone dose is established for the patient, a physician can monitor the patient for compliance with his or her prescribed dose by comparing the plasma methadone concentration of methadone, as calculated by the present method, with his expected, historical plasma methadone concentration for that particular methadone dose; hence, uncovering covert methadone diversion or supplementing.

Briefly described, the method of determining plasma methadone concentration from urine comprises the step of first determining whether the urine sample is indeed from the patient in question and whether or not it is adulterated. This can be done by comparing urine pH, specific gravity, and creatinine level with that of normal urine and specific values previously determined for the patient. If found to be unadulterated and probably from the patient in question, the urine methadone concentration is measured with standard quantitative laboratory methods, such as high pressure liquid chromatography or gas chromatography/mass spectrophotometry (GC/MS). Preferably, because of the ease and rapidity of analysis, florescence polarization immunoassay (FPIA) is employed such as with an Abbott TDX or ADX Analyzer.

Once an analytical value has been determined for the actual concentration of methadone in the sample, adjustments are made to account for the effects of variations in certain urinary parameters upon this concentration. A relationship exists between the actual concentration of methadone adjusted for compounding effects of urine specific gravity, the renal clearance of methadone as a function of urine pH, and the concurrent plasma methadone concentration. By obtaining multiple urine samples from a patient, once or twice a week, it is possible to establish a stable, baseline, 24-hour trough plasma methadone concentration for each patient against which a current or future value can be statistically compared.

Finally, given a patient's weight an estimate of the final daily methadone dose required by a patient can be determined. A previously developed empirical graph of plasma methadone concentration (ng/ml) versus daily oral methadone dose ingestion (mg/day) for the general population is utilized. This curve represents the 24 hour trough plasma methadone concentration expected for the average patient comprising the cohort from which the data were generated. For example, an average patient having a weight of 154 pounds (70 Kg) and an average methadone plasma half-life of 31.5±10.2 hours, normally ingesting methadone every 24 hours (approximate range 18–30 hours), and providing a second or later urine void of the day. In the event a particular patient falls outside the "average profile", it is a simple matter to adjust for these parameters in relating the patient's actual plasma methadone level to his average daily ingestion of methadone.

The actual urine methadone concentration may also be converted to a urinary parameter-normalized urine methadone concentration which is a constant and individual value for each patient. The calculation incorporates the measured actual urine methadone concentration, methadone dose, patient's weight, urine pH, and urine specific gravity. By establishing an individual's base value for the urinary parameter-normalized urine methadone concentration, subsequent readings may be compared with the base value to evaluate whether the patient is compliant with his or her prescribed dose.

Again, this is done by first determining whether the urine sample is adulterated as by comparing urine pH, specific

gravity and creatinine level with that of normal urine and previously established patient baseline values. If not adulterated, the actual urine methadone concentration is measured as previously described. The urinary parameter-normalized urine methadone concentration is next calculated as a function of the urine methadone concentration, methadone dose, patient's weight, urine specific gravity, and urine pH. Finally, a comparison of this value is made with a previously established individual's base value for urinary parameter-normalized urine methadone concentration.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a block diagram of a preferred method of the present invention, the last step being optional.

FIG. **2** is a block diagram of another preferred method of the present invention.

FIG. **3** is a graph of renal methadone clearance versus urine pH.

FIG. **4** is a graph of Reverse Urine Creatinine Excretion Factor versus Urine Volume Production Rate Factor.

FIG. **5** is a graph of Urine Volume Production Rate Factor versus Specific Gravity Factor.

FIG. **6** is a graph of plasma methadone concentration versus daily oral methadone dose.

FIG. **7** is a graph of plasma methadone concentration calculated using the method of the present invention versus measured plasma methadone concentration using Abbott FPIA.

FIG. **8** is a graph of urine methadone concentrations simultaneously measured by FPIA and GC/MS.

DETAILED DESCRIPTION OF THE INVENTION

Testing for Adulteration

First, a supervised, spot sample of urine is collected from a patient. Several properties of the urine are measured to evaluate whether the urine is adulterated, adulteration being the altering by a patient of his or her urine in an effort to prevent detection of illicit drug use or diversion of methadone. Adulteration typically is accomplished by adding foreign substances to the urine such as salt, bleach, or vinegar. Many patients attempt to dilute amount of drugs in the urine sample by drinking large quantities of water or by adding water to the sample. Adulteration may also occur by substituting another person's urine for the patient's own urine, including instillation of foreign urine into the patient's bladder.

In checking for adulteration, urine pH is measured, as with the use of a pH Data Logger type meter available from Oakton, to see if it is within the normally expected pH range of 4.5 to 8.5. Urine specific gravity (sg) is also measured to see if it is within the normal range of 1.004 to 1.035 units; a Digital Urinometer by Biovation may be used for this test. Creatinine, an end product of glycine and arginine metabolism excreted through the kidneys, is measured to evaluate renal function. The creatinine level in human urine usually ranges from 8 to 500 mg/dl, the range being affected by variables such as age, sex, diet, lifestyle and geographic location. Creatinine levels generally are homeostatically maintained by the body at a constant value for each individual patient over his or her lifetime. Creatinine levels may be determined on many different analyzers, including a TDx REA Creatinine System available from Abbott Laboratories. All of these tests are helpful in establishing normally expected ranges for each patient and the overall population of patients.

Once pH, specific gravity, and creatinine level values for the spot urine sample are obtained for a particular patient, comparisons can be made between the sample in question and values previously measured (if already available) both for the patient and for normals to ascertain whether the urine sample is adulterated. If no adulteration is found, a data base is created or extended for the patient so that a basis of comparison exists for future spot urine samples. Of the three measures, urinary creatinine level is generally the most useful indicator as to whether the spot sample is that of the patient or of someone else.

Determination of Raw Urine Methadone Concentration

The unadulterated sample is next analyzed for methadone concentration, preferably using Fluorescence Polarization Immunoassay (FPIA) technology. In this regard an Abbott TDX or ADX Analyzer may be profitably employed. Other standard analytical methods could also be used such as chromatography or other types of immunoassay. The value obtained is the raw urine methadone concentration of the patient, u.

Determination of Plasma Methadone Concentration

Plasma methadone concentration is obtained from the raw urine methadone concentration by utilizing a standard dimensionally correct relationship known as the renal clearance, which is,

$$cl=(u\cdot v)/p \tag{1}$$

where cl is renal clearance (ml/min), u is raw urine methadone concentration (ng/ml), v is the volume of urine collected in time (ml/min) or otherwise known as the urine volume production rate, and p is the measured plasma methadone concentration at the midpoint of the collection period (ng/ml).

Since the actual, current renal methadone clearance is not generally known for any one patient, nor can it easily be directly measured under normal clinic conditions, it must be estimated from an empirical relationship. It has now been found from actual experiments measuring urine and plasma methadone concentrations over timed collection periods (which recognizes that the renal clearance for methadone is strongly affected by urinary pH because of the weakly basic properties of methadone), that renal clearance relates to urine pH in the range 4.8–8.7 (see FIG. **3**) as,

$$cl=104{,}218\cdot pH^{(-4.76)} \tag{2}$$

and for which generally, a strong dependence upon actual patient weight is not noticed.

Rearranging Equation (1), the plasma concentration of urine may be calculated as follows,

$$p=u\cdot v/cl \tag{3}$$

The actual, raw urine methadone concentration is known from the FPIA results. Renal clearance can be calculated from Equation (2) by utilizing the urine pH previously measured in testing for adulteration. However, actual values of the urine volume production rate, v, are not available since routine clinical urine sampling procedures only provide a point-in-time or spot urine sample.

Persons skilled in the art state that it is not possible to calculate the plasma concentration of a drug from the spot urine sample; instead, a timed urine collection must be done (usually 24 hours). It has been found that these teachings are flawed and not grounded in fact.

It is now noted that renal excretion rates (mg/min) for drugs and urine metabolites are relatively constant for any patient during a typical day. This constancy has now been experimentally verified by looking at the renal excretion rates of methadone, benzodiazepines, other drugs and creatinine and other endogenous metabolites as a function of urine volume production rate. For example, using 12 compliant control subjects we have collected sequential, com-

plete and timed (1–8 hours holding periods) aliquots of urine over 24 to 72 hour periods. For each and every urine aliquot, urine volume production rate (ml/min), specific gravity and creatinine concentration (ng/ml) were determined.

Using this data, a dimensionless, linear relationship was found to exist, which is the same for each and every patient, between a urine volume production rate factor (UVPRF) and a reverse urine creatinine excretion factor (RUCEF). For each individual, control, urine collection period, the UVPRF is defined by the ratio of urine volume production rate for each urine aliquot collected, v, to the urine volume production rate for the most concentrated sample in the collection period with a specific gravity usually near 1.030, v',

$$UVPRF=v/v'. \tag{4}$$

The RUCEF factor is defined by the ratio of the creatinine concentration of the most concentrated urine aliquot with a specific gravity usually near 1.030, u', to the creatinine concentration for each urine aliquot collected, u,

$$RUCEF=u'/u. \tag{5}$$

This linear relationship is shown in FIG. 4. The best fit linear regression line is given by the expression,

$$RUCEF=0.942(SE\ 0.013)\cdot UVPRF+0.121(SE\ 0.043) \tag{6}$$

$$u'/u=0.942\cdot v/v'+0.121 \tag{7}$$

adjusted squared multiple R=0.985, standard error (SE) of estimate=0.242, F-ratio 4965.

Therefore, contrary to the traditional teachings of those skilled in the art, urine drug and metabolite concentrations, u, are inversely related to the volume of urine produced by the kidneys, v, clearly demonstrating that the product (u·v) is constant at any particular time point and urine pH (given a steady-state plasma methadone concentration p and renal clearance cl).

Since p, cl, and (u·v) at any time point and urine pH are constant, steady-state values, it follows that from Equation (7) some empirical mathematical relationship must exist between u and v such that given an arbitrary urine volume production rate v' and an equivalent u' at a reference point (specific gravity 1.030):

$$\{u\cdot v\}_{sg\ actual}=\{u'\cdot v'\}_{sg\ 1.030} \tag{8}$$

or upon rearrangement for u' gives,

$$u'=u\cdot(v/v') \tag{9}$$

where the products given in Equation (9) are those measured for a spot urine collected with an actual specific gravity and a corrected specific gravity typical of a morning void of 1.030.

Using controlled urine collections, we have measured a urine volume production rate v' of 0.44 ml/min for persons with reasonably normal renal functions at a specific gravity of 1.030. It has also been discovered that a linear relationship exists between the urine volume production rate factor and the specific gravity factor (SGF), {(1.030–1.000)/(sg–1.000)}, as shown in FIG. 5 and given below:

$$UVPRF=v/v'=2.43(SE\ 0.106)\cdot SGF-1.43(SE\ 0.216) \tag{10}$$

where the adjusted squared multiple R=0.856, standard error of the estimate=0.787, F-ratio 482.

Combining all of the above considerations, plasma methadone concentrations can be calculated by substituting Equations (2, 8, 9 and 10) in Equation (3):

$$\begin{aligned} p &= u\cdot v/cl \\ &= u'\cdot v'/cl \\ &= v'\cdot u\cdot(v/v')/cl \\ &= 0.44\cdot u\cdot(2.43\cdot SGF-1.43)/104{,}218\cdot pH^{(-4.76)} \end{aligned} \tag{11}$$

where values of u, specific gravity, and pH are known from previous test results on a patient's spot urine sample.

Comparing Patient's Calculated Plasma Methadone Concentration to that of an Average Patient for the Same Dose

Once the plasma methadone concentration is calculated from Equation (11), it is compared with the plasma methadone concentration expected from an average patient on a similar daily methadone dose as shown in FIG. 6, which demonstrates how plasma methadone concentration varies with dose for the standard population. FIG. 6 was developed by utilizing data from 8300 urine samples from 150 methadone maintenance patients on controlled daily methadone dosages.

Using this figure, a clinician can estimate how a prescribed dose will effect a patient's methadone plasma level. For example, a patient on a 70 mg/day methadone dose is expected from FIG. 6 to have a plasma methadone concentration of 200 ng/ml. However, from the spot urine sample the calculated plasma methadone concentration is 100 ng/ml thereby indicating that the patient's body is quickly metabolizing the methadone and a higher dose is needed, that the patient is diverting the methadone to others or that the patient is simply not using it. Higher concentrations per dose suggest the opposite of the above. Knowing that the plasma methadone concentration does not correlate to the prescribed methadone dosage, the clinician now has valuable information to evaluate the next step in the patient's program.

An optional use of the calculated plasma methadone concentration is to estimate the methadone dose that the patient has taken. FIG. 6 is used to estimate the patient's methadone dose by adjusting the calculated plasma methadone concentration relative to any parameters of the patient that fall outside the average patient parameters, such as patient body weight, methadone plasma half-life, and time of ingesting dose.

Verification

In order to ascertain the effectiveness of the plasma methadone concentration formulation, blood and urine samples were taken from a control group of patients. Urine and blood samples were simultaneously analyzed for plasma methadone concentration using FPIA and GC/MS. The urine methadone concentration was converted to a calculated plasma methadone concentration utilizing the formulation of the present invention in Equation (11).

Referring now to FIG. 7, the accuracy of calculating plasma methadone concentration from urine methadone concentration is verified by the excellent linear agreement between the plasma concentrations calculated by the present method from random, spot urine measurements and concurrently measured plasma methadone concentrations using actual blood samples: Estimated=0.970(SE 0.034)·Measured −1.25(SE 11.495), adjusted squared multiple R=0.987, standard error of estimate=20.155, F-ratio 810.

Determination of Urinary Parameter-Normalized Urine Methadone Concentration

The parameters of a patient's urine, such as pH and specific gravity, vary from one day to the next dependant upon the type and quantities of foods and beverages ingested. Additionally, individuals metabolizes these substances, as well as methadone, at different rates. To account for these variations, a urinary parameter-normalized urine methadone concentration, nu, is calculated that adjusts

measured raw urine methadone concentration, u, in accordance with a prescribed methadone dose, urine specific gravity, patient's current body weight (lbs) and urine pH. The relationship between u, pH, dose and specific gravity was empirically developed using nonlinear regression analysis. Results were normalized to a dose level of 80 mg/day, a patient weight of 154 pounds, and urine pH of 6.5 giving the final equation for monitoring a patient's nu:

$$nu=\{(80/DOSE)^{0.823}\}\cdot\{(6.5/pH)^{-4.838}\}\cdot(WGT/154)\cdot UVPRF\cdot u \quad (12)$$

The urinary parameter-normalized urine methadone concentration is statistically constant and unique for each patient regardless of an individual's methadone metabolism and daily changes in urine parameters. Thus, a patient's baseline nu, once established accurately for an individual patient within a statistical margin of error, may be used to evaluate methadone diversion or supplementation in patients by comparing subsequent calculations of this value with the patient's particular established baseline. If the subsequent calculation is similar to the established baseline, the patient is complying with his prescribed dose.

The generation of a patient's nu baseline value is done using standard statistical techniques developed for relating the mean and standard deviation observed from a particular sampling distribution (of size n elements) to the mean and standard deviation expected for the whole population of values, both for each patient and the population of all patients. For further details one can refer to the text, Hahn GJ, Meeker WQ, Statistical Intervals, John Wiley and Sons, 1991.

To utilize such techniques it is first necessary to determine what the expected standard deviation is for the whole population of compliant patients under observation. Previously, it had been observed that although means value for nu are different for each patient, the observed variability about the mean for compliant patients is quite consistent and similar to the overall cohort of compliant patients; suggesting that the following statistical technique may be utilized.

Sequential, urine data was retrieved from computer files for 216 patients (13,000 data points) and transferred into a commercial statistical/graphical package produced by Systat, Inc. Each patient's data was sorted individually by ascending concentration for initial data review. All data points having unusual creatinine values <10 or >500 mg/dl or a methadone concentration <300 or >60,000 ng/ml were discarded as being suspect and non-physiologic. Additional outliers were eliminated from each patient file using manual review (preliminary statistic data were available as a guide). For statistical reasons, all patients having less than 10 acceptable data points were also eliminated.

Using the remaining data sets for each patient (180 persons, approximately 12,000 individual urine values), individual nu values were obtained from which individual means and standard deviations were calculated (method shown later).

Utilizing this data, a plot of sample size (for each patient) versus calculated sample standard deviation (for each patient) was generated. Approximately, 180 individual, standard deviations (y-axis) were plotted against samples sizes ranging from 10 to 200 (x-axis). Using standard 95% confidence limit tables from Hahn and Meeker, lower and upper limits were co-plotted on the above curve by adjusting the overall population standard deviation until the data bounded by the prediction curves enclosed all acceptable data. The average population standard deviation for the set of acceptably, compliant patients was found to be about 3000 for this particular set of patients, though it could be lower if further restrictions to the initial data set were applied.

Given this value, another set of prediction equations specifying the allowable range for the next measured nu for a particular patient, given a sample size of n, a mean nu for an individual patient and either the patient standard deviation or the population standard deviation (whichever is least), can be calculated as shown in Hahn and Meeker. If the measured value is within the acceptable statistical range, given a previously calculated mean and standard deviation, then it is accepted. If the value is too high or too low, this is marked on the urine drug screen under the column called Pred as shown in clinical cases #'s 4 and 5.

An alternative method which can be used to establish outliers for each patient data set, though less rigorous than the statistical method, is simply to specify a + and − range about the mean, say +/− 50% of an individual patient's mean. This simple method can give satisfactory and reasonable results.

Verification

Shown in Table 1 is a partial representation of data from a standard computer printout for a compliant patient in which is summarized both urine parameters and methadone concentrations. The last column in the figure represents the urinary parameter-normalized urine methadone concentration values for the patient which are quite constant once sg, pH, dose corrections are made to the raw urine methadone concentration.

TABLE 1

Date	Dose	Temp	pH	SG	CR	u	p	nu
04-20-92M	70	98.0	5.40	1.022	335	6838	167	6966
04-15-92W	70	96.0	5.70	1.024	268	6536	176	7381
04-13-92M	70	96.0	5.90	1.019	271	5462	259	10913
04-10-92F	70	98.0	5.70	1.021	377H	5180	177	7430
04-06-92M	70	98.0	5.90	1.028	261	7398	171	7208
04-02-92h	70	96.0	5.70	1.026	271	5990	149	6254
03-30-92M	70	94.0	5.60	1.021	303	4203	132	5532
03-25-92W	70	98.0	5.20	1.021	271	8469	187	7790
03-24-92T	70	98.0	6.00	1.023	243	3736	139	5852
03-20-92F	70	96.0	5.80	1.024	272	5601	164	6881
03-16-92M	60	94.0	5.30	1.022	286	7049	157	7448
03-13-92F	60	96.0	5.70	1.019	277	4935	199	9473
				Mean:	286	5950	173	7427
				SD:	37	1372	33	1492
				CV:	12.7	23	19.1	20
				Tests:	12	12	12	12

Clinical Examples

Case #1: J. S. is a 52 year old woman with right-sided, migraine with aura headaches beginning after her hysterectomy at age 44 and prior to regular use of any medication. Her migraines begin with flashes of light and blurry vision in either eye. Often "a film covers my right eye." Prodromata are usually followed by right retro-orbital pain accompanied by photophobia and nausea. This patient also suffers tension headaches and headaches secondary to allergic rhinitis. She is able to clinically differentiate migraine and tension components of her headaches, as the migraine component is refractory to multiple trials of ergot alkaloids, benzodiazepines, NSAIDs, beta-blockers, calcium channel blockers and psychotherapy. Multiple CT scans have been normal.

J.S. had been biochemically dependent upon prescription opioids to relieve migraine pain for over a year prior to her referral to a methadone maintenance clinic. According to Federal Register 21 CFR Part 291, a person biochemically dependent (this is the current definition for opioid dependency utilized by the federal government) to narcotics for more than a year qualifies to enter into a methadone maintenance program.

J.S.'s situation is similar to that of approximately 0.5% of the general, adult population of the United States who are

also biochemically dependent upon opioid medications because of legitimate medical illness and disease. Oftentimes, it is difficult for the clinician to determine whether or not the patient is currently using opioids for relief from organic pain or is treating the psychological sequelae of their disability. In either case, methadone maintenance is the most efficacious choice to help and protect the patient.

J.S. enrolled in the methadone maintenance program 36 months ago for pain management. Gradual titration to 35 mg of methadone was achieved over a short time period during which migraines slowly decayed in frequency and severity. During her time in treatment she has subsequently suffered only 2 migraine attacks which were greatly reduced in intensity. Both attacks were related to a transient decrease in plasma methadone levels below 80 ng/ml secondary to vomiting associated with viral syndromes.

A typical urine history is shown in Table 2 for this patient showing both estimated plasma methadone levels and the urinary parameter-normalized methadone concentration.

TABLE 2

Date	Dose	Temp	pH	SG	CR	u	p	nu
07-01-93h	45	94.0	7.70	1.012	319	1069	348	21153
06-21-93M	45	94.0	6.90	1.008	265	1336	426	25720
06-14-93M	45	94.0	6.60	1.011	273	2109	368	22145
06-07-93M	45	95.0	7.30	1.011	270	1883	532	32208
06-03-93h	45	98.0	7.00	1.010	254	646	168	10174
05-27-93h	45	94.0	7.60	1.018	269	1246	215	13051
05-20-93h	45	95.0	6.80	1.011	275	1285	259	15585
05-13-93h	45	95.0	7.80	1.011	272	757	293	17845
05-03-93M	45	97.0	5.50	1.020	357H	4094	128	7585
04-29-93h	45	94.0	6.70	1.014	N/T	1318	180	10815
04-22-93h	45	96.0	6.80	1.020	320	3900	335	20168
04-12-93M	45	94.0	7.20	1.009	260	915	310	18777

TABLE 2-continued

Date	Dose	Temp	pH	SG	CR	u	p	nu
				Mean:	285	1713	297	17936
				SD:	32	1146	116	7042
				CV:	11.3	66.8	39	39.2
				Tests:	11	12	12	12

Case #2: A.N. is a 44 year old woman whose migraine with aura began approximately 20 years ago. Beginning with blurred vision, subsequent unilateral headaches are invariably accompanied by nausea and vomiting, photophobia, and hypersensitivity to motion of her head and to cigarette smoke. Despite trials of biofeedback, physical therapy, and medications (trials of beta blockers, calcium channel blockers, ergot alkaloids over the years) and drug holidays; the frequency of her headaches has increased over the years to nearly daily occurrence. Lumbar punctures and multiple CT and MRI scans of her head were normal.

Following failure of self-administered IM administration of nalbuphine to control her pain, she began methadone maintenance 24 months ago. Because of many years of prior use of barbiturate-containing compounds her hepatic metabolic function was significantly enhanced requiring more than normal amounts of methadone—as shown by urine plasma concentration estimates. After stabilization on 130 mg per day of methadone, her migraines ceased completely at a plasma methadone level above 135 ng/ml. She continues to experience infrequent stress-related headaches, which are slowly decreasing in severity and frequency.

Urine histories are shown for this patient in Tables 3 and 4. Notice how plasma methadone levels have increased in this patient over time as hepatic function returned to normal by discontinuing barbiturate-containing compounds (bar).

TABLE 3

Date	Dose	Temp	pH	SG	CR	bar	u	p	nu
06-01-91S	100	N/T	5.10	1.021	200	HI	6338	127	3243
05-29-91W	100	N/T	5.40	1.021	184	2370	1985	52	1339
05-25-91S	100	N/T	5.40	1.020	N/T	N/T	1360	39	995
05-22-91W	100	N/T	5.10	1.013	N/T	N/T	1511	62	1582
05-20-91M	100	N/T	5.10	1.005	134	HI	615	80	2026
05-18-91S	100	N/T	5.40	1.017	N/T	N/T	2067	76	1952
05-15-91W	80	N/T	5.40	1.019	129	HI	1120	35	1070
05-13-91M	65	N/T	5.70	1.009	72	HI	335	37	1367
05-11-91S	65	N/T	5.10	1.016	182	HI	816	25	911
05-08-91W	50	N/T	5.40	1.010	N/T	N/T	853	65	2924
05-06-91M	40	N/T	5.40	1.019	N/T	N/T	174	5	LOW
05-03-91F	40	N/T	5.40	1.009	89	HI	296	26	1389
				Mean:	141		1456	52	1591
				SD:	49		1661	32	840
				CV:	35.0		114	62.3	52.7
				Tests:	12		12	12	12

TABLE 4

Date	Dose	Temp	pH	SG	CR	bar	u	p	nu
04-04-92S	130	95.0	5.80	1.013	196	0	4915	373	7728
03-28-92S	130	98.0	5.90	1.020	210	0	6565	287	5944
03-21-92S	110	95.0	5.50	1.021	216	0	9651	278	6580
03-14-92S	110	97.0	5.70	1.022	210	0	8964	282	6703
03-07-92S	110	96.0	6.30	1.014	186	0	4471	455	10880
03-02-92M	110	95.0	5.60	1.022	206	0	8778	254	6025
02-21-92F	120	96.0	6.20	1.016	181	0	5169	403	8970
02-15-92S	120	98.0	5.90	1.015	187	0	4525	306	6778

TABLE 4-continued

Date	Dose	Temp	pH	SG	CR	bar	u	p	nu
02-08-92S	120	96.0	6.10	1.017	181	0	5506	364	8074
01-31-92F	120	95.0	6.20	1.016	218	0	6896	538	11966
01-18-92S	120	96.0	5.50	1.021	224	0	9503	274	6031
01-11-92S	130	96.0	5.30	1.020	182	0	9494	249	5117
				Mean:	206	0	7036	399	7566
				SD:	16	0	2114	90	2095
				CV:	8.0	0	30	26.5	27.6
				Tests:	12	12	12	12	12

Case #3: Shown in Table 5 are examples of estimated plasma methadone levels for four patients demonstrating how to detect misuse of methadone.

TABLE 5

Utilization of Plasma Methadone Levels
To Uncover Misuse of Methadone
Estimated Plasma Methadone Concentration (ng/ml), p

Sample	Patient A*	Patient B	Patient C***	Patient D
1	480	346	89	1247****
2	465	234	44	1173****
3	485	281	50	1061****
4	525	233	334	1343****
5	454	376	84	435
6	410	208	310	575
7	531	290	778	427
8	483	172**	800	514
9	403	0**	33	474

*Patient A ingests 90 mg/day of methadone q 24 hr. as instructed. He ingests a does in the clinic on Mon., Wed. and Fri., mean 24-hr. though level is 470 ng/ml with a CV = 9.4%.
**Patient B receives 80 mg/day of methadone. She only gets a take home dose for Sunday. Expected mean value (samples 1–6) is 281 +/– 62 ng/ml. Sample 8 was taken 48 hr. after her last dose providing an estimate of plasma methadone half-life of about 65 hrs.
Sample 9 is an example of substitution on a non-patient urine sample.
***Patient C ingests 50 mg/day in clinic on Mon., Wed. and Fri. Her expected plasma concentration should be about 170 ng/ml. She is likely diverting Tues, Thur. and Sun. take home doses and spiking urines with exogenous methadone on other days. Solution was to withdraw take home doses.

TABLE 5-continued

Utilization of Plasma Methadone Levels
To Uncover Misuse of Methadone
Estimated Plasma Methadone Concentration (ng/ml), p

Sample	Patient A*	Patient B	Patient C***	Patient D

****patient D currently ingests 100 mg/day of methadone (samples 5–9). Previously, he was ingesting over 200 mg/day of methadone via supplementing with illicit methadone (samples 1–4). Solution was to slowly taper him back to 100 mg/day on a daily basis of clinic visits.

Cases #4 and #5

Shown in Tables 6 and 7 are data demonstrating how the statistical program is utilized by the computer to 'flag' a urine methadone value as being outside the acceptable range for the patient. Armed with this data, it is possible for a healthcare provider to speak with the patient about this abnormality before it becomes a continuing problem. Typically, lab errors are ruled out prior to discussion with the patient. Assuming no laboratory explanation is forthcoming, the healthcare provider can consider substitution of urine by the patient (often noted by variation in measured urinary parameters, including normalized creatine); ingestion of methadone on a non-24 hour basis; ingestion of additional and unapproved methadone; selling of take-home methadone doses; taking a medication interfering with the metabolism of methadone and so forth. Having an objective and quantitative methadone history to present to the patient overcomes the natural tendency for many patients to be untruthful.

TABLE 6

Date	Dose	Temp	pH	SG	CR	u	p	nu	Pred
09-10-93F	140	95.0	7.11	1.013	307	3631	727	17073	High
09-08-93W	140	95.0	5.19	1.025	306	12847	204	4686	
09-02-93h	140	95.0	5.49	1.023	317	6345	154	3555	
08-30-93M	140	95.0	4.68	1.023	316	12629	144	3269	
08-26-93h	140	95.0	4.91	1.020	224	10227	186	4251	
08-23-93M	120	94.0	4.91	1.025	239	14105	172	4466	
08-20-93F	120	94.0	5.78	1.028	299	8194	172	4511	
08-17-93T	120	94.0	5.31	1.026	311	8814	145	3768	
08-13-93F	120	94.0	6.18	1.013	357	3101	318	8401	
08-10-93T	120	95.0	5.81	1.021	296	4634	173	4550	
08-06-93F	120	95.0	6.69	1.019	243	2923	252	6696	
08-03-93T	120	95.0	5.53	1.024	185	8645	201	5264	
				Mean:	283	8008	237	6874	
				SD:	49	3945	162	3803	
				CV:	17.3	49.2	68.3	64.7	
				Tests:	12	12	12	11	

TABLE 7

Date	Dose	Temp	pH	SG	CR	u	p	nu	Pred
08-06-93F	130	96.0	4.88	1.025	49L	4305	51	1858	LOW
08-02-93M	130	96.0	4.81	1.024	215	13601	163	5922	
07-29-93h	130	96.0	5.05	1.019	211	11015	249	9089	
07-26-93M	130	95.0	LOW	1.014	214	8822	163	5865	
07-22-93h	130	96.0	4.52	1.028	42L	4431	29	1042	LOW
07-19-93M	130	95.0	4.66	1.021	258	25400	333	12050	
07-15-93h	130	96.0	5.96	1.003	LOW	5585	2642	97615	HIGH
07-12-93m	130	96.0	4.76	1.021	228	14361	208	7550	
07-09-93F	130	94.0	4.76	1.015	230	10940	266	9663	
07-06-93T	130	96.0	5.20	1.024	249	17816	309	11313	
07-01-93h	130	96.0	5.10	1.012	224	6963	319	11630	
06-28-93M	130	97.0	LOW	1.011	241	7478	190	6841	
06-24-93h	130	N/T	LOW	1.009	232	6889	224	8088	
				Mean:	214	10585	396	14502	
				SD:	41	6037	681	25203	
				CV:	19.1	57	172	173.7	
				Tests:	12	13	13	13	

Case #6 Methadone concentration data were simultaneously measured using GC/MS and FPIA for urine obtained from five patients and plotted in FIG. 8 for comparison. Linear regression analysis shows that GCMS =0.97FPIA =48, R=0.999: both methods are essentially equivalent. Similarly, methods other than GC/MS or FPIA could also be used, such as gas chromatography, high pressure liquid chromatography, chemical methods and so on, to sequentially follow raw urine methadone concentration patient data for utilization in this invention.

Conclusion

It is thus seen that methods are now provided for monitoring opioids addicted patients who have been placed on methadone maintenance programs for compliance without the need to draw blood for determining plasma methadone concentration. The inventive methods are clinically practical without high laboratory testing cost, the invasiveness of withdrawing blood and the attendant exposure to medical professionals of patient blood having high probability of hepatitis and HIV infection.

While the invention has been described in detail with particular reference to the preferred methods thereof, it should be understood that many modifications, additions and deletions may be made thereto without departure from the spirit and scope of the invention as set forth in the following claims.

What is claimed is:

1. A method of monitoring compliance of a patients that has been placed on a methadone maintenance program which comprises the steps of

(a) obtaining a sample of the patient's urine,

(b) measuring the concentration of methadone, the specific gravity and the pH value of the urine sample,

(c) calculating the concentration of methadone of the plasma as a function of the measured concentration of methadone of the urine, urine specific gravity, and urine pH, and

(d) comparing the calculated concentration of methadone of the plasma with an expected value for the maintenance program prescribed.

2. The method of claim **1** wherein the urine sample is also tested for adulteration.

3. The method of claim **2** wherein testing for adulteration comprises measuring the creatinine level of the urine sample and comparing the measured creatinine level with a predetermined normal level of creatinine of the patient.

4. The method of claim **1** wherein step (b) the concentration of methadone is measured by fluorescence polarization immunoassay.

5. The method of claim **1** wherein step (c) the concentration of methadone of the plasma is calculated in accordance with the equation

$$p = k_1 \cdot u \cdot (k_2 \cdot SGF - k_3) / k_4 \cdot pH^{k5}$$

where p is the calculated plasma methadone concentration, u is the measured urine methadone concentration, SGF is the specific gravity factor of the patient's urine, pH is the measured pH value of the urine, and k_1, k_2, k_3, k_4 and k_5 are constants.

6. A method of monitoring compliance of a patient that has been placed on a methadone maintenance program with a prescribed methadone dose which comprises the steps of

(a) obtaining a sample of the patient's urine,

(b) measuring the concentration of methadone, the specific gravity and the pH value of the urine sample,

(c) calculating a normalized urine methadone concentration as a function of the measured urine methadone concentration, prescribed methadone dose, urine specific gravity, and urine pH, and

(d) comparing the present normalized urine methadone concentration with a previously determined historical base values for the patient's normalized urine methadone concentration to verify compliance;

whereby if the patient is in compliance with his/her prescribed dose, the present and historical base values of the patient's normalized urine methadone concentration are similar.

7. The method of claim **6** wherein the urine sample is tested for adulteration.

8. The method of claim **7** wherein testing for adulteration comprises measuring the creatinine level of the urine sample and comparing the measured creatinine level with a predetermined normal level of creatinine of the patient.

9. The method of claim **6** wherein step (b) the concentration of methadone is measured by fluorescence polarization immunoassay.

10. The method of claim **6** wherein step (c) the normalized urine methadone concentration is calculated in accordance with the equation:

$$nu=\{(k_1/DOSE)^{k7}\}\cdot\{(k_3/pH)^{-k4}\}\cdot(WGT/k_5)\cdot(k_6\cdot SGF-k_7)\cdot u$$

where nu is the calculated normalized urine methadone concentration, DOSE is the prescribed methadone dose, pH is the pH of the spot urine sample, SGF is the specific gravity factor of the patient's urine, u is the measured urine methadone concentration of the spot urine sample, WGT is the current patient's body weight, and k_1–k_7 are constants.

11. A method of determining plasma methadone concentration from urine which comprises the steps of

(a) obtaining a sample of the patient's urine,

(b) measuring the concentration of methadone, the specific gravity and the pH value of the urine sample, and

(c) calculating the concentration of methadone of the plasma as a function of the measured concentration of methadone of the urine, urine specific gravity, and urine pH.

12. The method of claim 11 wherein the urine sample is also tested for adulteration.

13. The method of claim 12 wherein testing for adulteration comprises measuring the creatinine level of the urine sample and comparing the measured creatinine level with a predetermined normal level of creatinine of the patient.

14. The method of claim 11 wherein step (b) the concentration of methadone is measured by fluorescence polarization immunoassay.

15. The method of claim 11 wherein step (c) the concentration of methadone of the plasma is calculated in accordance with the equation

$$p=k_1\cdot u\cdot(k_2\cdot SGF-k_3)/k_4\cdot pH^{k5}$$

where p is the calculated plasma methadone concentration, u is the measured urine methadone concentration, SGF is the specific gravity factor of the patient's urine, pH is the measured pH value of the urine, and k_1, k_2, k_3, k_4 and k_5 are constants.

16. The method of claim 6 further comprising the step of measuring the patient's body weight, and wherein calculating the normalized urine methadone concentration also as a function of the measured patient's body weight.

* * * * *

EXHIBIT C

Ameritox, Ltd.

9930 W Hwy 80, Midland, TX 79706
Phone: 866-287-7584
Fax: 432-561-8619

Location: Ameritox Test Client 999
Address: 9930 West Hwy 80 Midland, TX 79705
Fx: (432) 561-8619
Physician: DR. BACKER

Patient Name: TESTERSON, TEST
Birth Date: 12/31/1980
Height: 72
Weight: 225
Gender: Male
Patient ID:

Accession: P040403
Lab Accession: 7061300003
Date Collected: 04/03/2007
Received By Lab: 04/04/2007
Reported:

Test Ordered (ng/ml)	Lab Result	Assay Cutoff	Normalized Value	Expected Low	Range High	Range Interpretation	Medication Interpretation
Amphetamines FPIA Class	12225	1000	28201.90				INCONSISTENT
Amphetamine by GCMS	2336	125					INCONSISTENT
Methamphetamine by GCMS	>8000	125					INCONSISTENT
Barbiturates	Negative	300					
Benzodiazepines	Negative	100					
Methadone	Negative	150					
Propoxyphene	Negative	200					
Opiates FPIA Class	110230	50	213541.08	85	290	NORMHI	Consistent
Codeine by GCMS	Negative	100					Consistent
Morphine by GCMS	100253	100					INCONSISTENT
Hydrocodone by GCMS	Negative	100					Consistent
Hydromorphone by GCMS	Negative	100					Consistent
Oxycodone by GCMS	NEGATIVE	100					INCONSISTENT
Oxymorphone by GCMS	NEGATIVE	100					INCONSISTENT
Oxycodone by EIA	NEGATIVE	100					INCONSISTENT
Cocaine	Negative	200					
Phencyclidine	Negative	25					
Cannabinoids	Negative	30					
Methadone Metabolite (EDDP)	Negative	150					
Other:							
Creatinine - Urine	98.36			5	300		
PH - Urine	7.3			3	11		
Specific Gravity - Urine	1.018			1.003	1.035		

Prescribed Drug	Drug Name	Drug Class	Dose (mg)	Freq (Low / High)	# Dose (Low / High)	PRN
PERCOCET	ACETAMINOPHEN		10	TID / TID	1 / 2	N
...	OXYCODONE	Opiates	10	TID / TID	1 / 2	N
DURAGESIC	FENTANYL	Fentanyl	2.4	Q72 / Q72	1 / 1	N

NORMHI: One or more normalized values were higher than expected. Please verify patient height, weight and prescription information.

> : Results that are shown with a > symbol next to the quantitative value are above the upper limit of quantitation.

The normalizations of drug immunoassays by FPIA are based on standard lean body mass calculations and specific properties of the drug of interest, e.g. hydrocodone, morphine, etc. These normalizations are compared to ranges based on known compliant patients using similiar calculations (+/-) a percentage of an average. The normalizations are only meant to be used as a guide in conjunction with all other measured data, (GC/MS data,

9930 W Hwy 80, Midland, TX 79706
Phone: 866-287-7584
Fax: 432-561-8619

Ameritox, Ltd.

Location:	Ameritox Test Client 999	**Patient Name:**	TESTERSON, TEST	**Accession:**	P040403
Address:	9930 West Hwy 80 Midland, TX 79705	**Birth Date:**	12/31/1980	**Lab Accession:**	7061300003
		Height:	72	**Date Collected:**	04/03/2007
	Fx: (432) 561-8619	**Weight:**	225	**Received By Lab:**	04/04/2007
		Gender:	Male	**Reported:**	
Physician:	DR. BACKER	**Patient ID:**			

Specific gravity, creatinine, and pH) and other clinical and behavioral information known to the treating physician. Due to many factors no single method can be accurate for all individuals.

***** End of Report *****

Ameritox, Ltd.

9930 W Hwy 80; Midland, TX 79706
Phone: 866-287-7584
Fax: 432-561-8619

Location:	Ameritox Test Client 999	**Patient:**	TESTERSON, TEST	**Accession:**	P040403
		Birth Date:	12/31/1980	**Lab Accession:**	7061300003
Address:	9930 West Hwy 80 Midland, TX 79705 Fax: (432) 561-8619	**Height:**	72	**Date Collected:**	04/03/2007
		Weight:	225	**Received by Lab:**	04/04/2007
		Gender:	Male	**Reported:**	04/16/2007
Physician:	DR. BACKER	**Patient ID:**	N/A		

Supplemental Explanation Report

Test / Drug Class / Medication	Explanation
Amphetamines	THE GC/MS RESULTS CONFIRM THE PRESENCE OF METHAMPHETAMINE & ITS METABOLITE AMPHETAMINE. METHAMPHETAMINE COMES IN TWO FORMS, THE d AND THE l ISOMER. A SPECIALIZED TEST IS AVAILABLE TO DIFFERENTIATE BETWEEN THE TWO FORMS.
Opiates	MORPHINE IS INDICATIVE OF USE OF MORPHINE, CODEINE METABOLISM, POPPY SEEDS OR HEROIN. DETECTION TIME FOR OPIATES IS 2-4 DAYS.
Opiates - Oxycodone	THE IMMUNOASSAY RESULT IS NEGATIVE FOR OXYCODONE. THIS INDICATES IT HAS BEEN SEVERAL DAYS SINCE THE LAST DOSE OF PERCOCET.

***** End of Report *****

EXHIBIT D

BELL BOYD
BELL, BOYD & LLOYD LLP

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Chicago, Illinois 60602-4207
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VIA EMAIL

August 6, 2007

Joel T. Galanter
Adams and Reese LLP
424 Church Street
Suite 2800
Nashville, Tennessee 37219

Re: *Ameritox et al. v. Aegis Sciences Corp.*, Case No. 07-80498 (S.D. Fl.)

Dear Mr. Galanter:

Your client, Aegis, currently advertises a "patented" program in connection with the offering of its drug testing services. Specifically, Aegis advertises its "Targeted High School Drug Testing Program" as including "Aegis' patented Zero-Tolerance Drug Testing process for common drugs of abuse...." *See* www.aegislabs.com/schools.asp.

Please identify, no later than close of business August 10, 2007, the patent number under which Aegis is advertising its Zero-Tolerance Drug Testing process.

Best regards,

Michael R. Osterhoff

mro:jqk

EXHIBIT E

ADAMS AND REESE LLP

Attorneys at Law
Baton Rouge
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Mobile
Nashville
New Orleans
Washington, DC

Joel T. Galanter
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joel.galanter@arlaw.com

August 8, 2007

By Email
Michael R. Osterhoff
Bell, Boyd & Lloyd LLP
70 West Madison Street, Suite 3100
Chicago, IL 60602-4207
mosterhoff@bellboyd.com

Re: Aegis Sciences Corp.

Dear Mr. Osterhoff :

Thank you for your letter August 6, 2007. As you may know, Zero Tolerance Drug Testing is a registered trademark of Aegis and is not patented. Non-lawyers (and even non-intellectual property lawyers) often fail to properly distinguish between trademarks, copyrights and patents and that appears to be what happened in this instance. Having had this error (located on a website page related solely to drug testing services for public and private high schools; a field in which your client is not a competitor) brought to its attention, Aegis rectified it on August 6, 2007, immediately after receiving your letter.

Aegis does not advertise or promote its Zero Tolerance Drug Testing program as a patented process. With the exception of the now corrected instance you brought to our attention, Aegis' sales and marketing materials do not refer to it as patented, and none of the many other pages discussing the Zero Tolerance Drug Testing program on Aegis' website refer to is as such.

If you are aware of any customers or potential customers that have viewed this webpage before it was corrected and believe that they may have been confused by it, please let me know who they are as Aegis will send a similar letter notifying them of its inadvertent error and the correction of it. If you are not aware of any such instances, I trust that this fully resolves this issue.

Sincerely yours,

Joel T. Galanter

EXHIBIT F

DRUG-FREE SCHOOLS

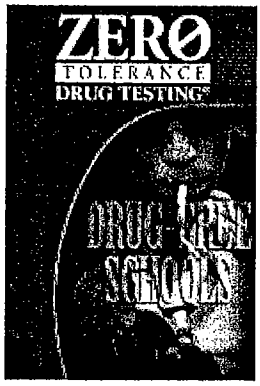
AEGIS SCIENCES CORPORATION

CHOOSE YOUR PATH :
Choose Your Path >>

SEARCH :
GO

Services for Public and Private High Schools

Targeted High School Drug Testing Program
In response to the growing concern about anabolic steroid use in High Schools, Aegis has recently announced the launch of a new **Targeted High School Drug Testing Program** designed for public and private high schools. The **Targeted Program** is designed to give high schools an affordable option for detecting and deterring steroid abuse in their athletic programs. The program also includes Aegis' patented Zero-Tolerance Drug Testing process for common drugs of abuse, the most accurate drug test available and the only test designed to test children. Contact Client Services for more information.



Keeping Schools Drug Free

Why Choose Aegis?
AEGIS is a federally certified (SAMHSA) laboratory that has provided policy development and drug-testing services to public and private high schools throughout the U.S. since 1986. Onsite testing devices and routine testing developed for workplace programs and offered by other laboratories miss 60-70% of detectable drug use! Only **AEGIS** can offer the most accurate drug test available: **Zero-Tolerance Drug Testing®** .

Zero-Tolerance Drug Testing®
Zero-Tolerance Drug Testing® is the only drug testing method specifically designed to test children. Zero-Tolerance® is superior to routine testing offered by other laboratories AND on site testing devices in the following ways:

- Zero-Tolerance® detects drugs at lower test thresholds.
- Zero-Tolerance® detects drugs such as: Ecstasy, Eve, MDA, PMA, OxyContin® , Lortab® , Percocet® , Vicodin® , and many others that go undetected by onsite devices and routine testing offered by other laboratories.
- Zero-Tolerance® detects drugs for a longer period of time: generally 2 -3 times longer than onsite devices and routine testing.
- Zero-Tolerance® is more resistant to adulteration. Lower test thresholds combined with advanced screening technology make Zero-Tolerance® unaffected or significantly less affected by products available at nutrition centers and on the Internet designed to "Beat the Test." (e.g. www.clearchoiceofny.com)

Anabolic Steroid Testing
The non-medical use of drugs by athletes to enhance performance is a serious problem, as well. Nutritional supplement use is on the rise and many of these products contain dangerous substances such as Nandrolone and Ephedrine. **AEGIS** is one of a few select laboratories testing for performance enhancing compounds such as Anabolic Steroids, Stimulants (including Ephedrine), Narcotics, and many others.

Services Included with all Test Profiles:
The following services are included with all drug-testing profiles at no additional fee:

- Policy development and review
- Collection kit & preprinted chain -of -custody form
- Overnight sample shipment
- Screening & confirmation for drugs of abuse and adulterants

- Electronic results reporting (Email, Efax, Fax)
- Random program administration
- Results consultation and interpretation with AEGIS Ph.D. Toxicologists

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Related Links

- Substance Abuse & Mental Health Services Administration
- Zero-Tolerance Drug Testing
- AEGIS Drugs of Abuse Info Page
- White House Office of National Drug Control Policy
- DEA Drug Abuse Information Page

<< Back

Page Last Updated: 4/23/2007 4:21:12 PM

EXHIBIT C

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA

AMERITOX, LTD. and U.D. TESTING, INC.,	)	
Plaintiff and Counter-Defendant	)	
v.	)	Case No. 07-80498-civ-MARRA
AEGIS SCIENCES CORP.,	)	
Defendant and Counter-Plaintiff.	)	

ANSWER TO FIRST AMENDED COMPLAINT AND COUNTERCLAIM

Defendant Aegis Sciences Corp. ("Aegis") answers the First Amended Complaint ("Complaint") filed against it by Ameritox, Ltd. ("Ameritox") and U. D. Testing, Inc. ("UDT") as follows:

1. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegation of paragraph 1 of the Complaint.

2. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegation of paragraph 2 of the Complaint.

3. Aegis admits it is a Tennessee corporation having its principal place of business at the address stated in the Complaint. Aegis denies it is it is offering for sale, selling, and using an infringing method in the United States or the Southern District of Florida.

4. Aegis denies the allegations contained in the first sentence of paragraph 4 of the Complaint. United States Patent Nos. 5,908,788 and 6,124,136 (respectively the "'788 Patent" and "'136 Patent," and collectively the "Patents in Suit") speak for themselves. The remaining allegations of paragraph 4 of the Complaint are legal conclusions to which no response is required. To the extent paragraph 4 contains additional factual allegations, they are denied.

5. The allegations contained in paragraph 5 of the Complaint are legal conclusions to which no response is required. To the extent that paragraph 5 contains factual allegations, they are denied.

6. The allegations contained in paragraph 6 of the Complaint are legal conclusions to which no response is required. To the extent that paragraph 6 contains factual allegations, they are denied.

7. Exhibit A, referenced in paragraph 7 of the Complaint, speaks for itself. The remaining factual assertions contained in paragraph 7 of the Complaint are denied.

8. Exhibit B, referenced in paragraph 8 of the Complaint, speaks for itself. The remaining factual assertions contained in paragraph 8 of the Complaint are denied.

9. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 9 of the Complaint.

10. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 10 of the Complaint.

11. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 11 of the Complaint.

12. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 12 of the Complaint.

13. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 13 of the Complaint.

14. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 14 of the Complaint.

15. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 15 of the Complaint.

16. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 16 of the Complaint. Exhibit C, referenced in paragraph 16 of the Complaint, speaks for itself.

17. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 17 of the Complaint.

18. Admitted.

19. Denied.

20. Denied.

21. Denied.

22. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations contained in the first sentence of paragraph 22 of the Complaint, the second sentence is denied.

23. Denied.

24. The first sentence of paragraph 24 of the Complaint is admitted, the second sentence is denied.

25. Denied.

26. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 26 of the Complaint.

27. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 27 of the Complaint.

28. Denied.

COUNT I
Patent Infringement of U.S. Patent No. 5,908,788

29. Aegis incorporates by reference, as if fully set forth herein, its answers to paragraphs 1 through 28 of the Complaint.

30. Denied.

31. Denied. Plaintiffs have never requested or demanded that Aegis cease using any method, and therefor cannot have any information or reasonable belief regarding Aegis' intentions. Further, Aegis has never used, sold and/or offered for sale the methods in the '788 Patent and therefor cannot cease such conduct. Aegis never would use, sell and/or offer for sale the methods in the '788 Patent because such methods are junk science.

32. Denied.

33. Denied.

34. Denied.

COUNT II
Patent Infringement of U.S. Patent No. 6,124,136

35. Aegis incorporates by reference, as if fully set forth herein, its answers to paragraphs 1 through 34 of the Complaint.

36. Denied.

37. Denied. Plaintiffs have never requested or demanded that Aegis cease using any method, and therefor cannot have any information or reasonable belief regarding Aegis' intentions. Further, Aegis has never used, sold and/or offered for sale the methods in the '136 Patent and therefor cannot cease such conduct. Aegis never would use, sell and/or offer for sale the methods in the '788 Patent because such methods are junk science.

38. Denied.

39. Denied.

40. Denied.

COUNT III
Florida Deceptive and Unfair Trade Practices Act

41. Aegis incorporates by reference, as if fully set forth herein, its answers to paragraphs 1 through 40 of the Complaint.

42. Denied.

43. Denied.

44. Denied.

45. Denied.

COUNT IV
Tortious Interference with Business Relationships

46. Aegis incorporates by reference, as if fully set forth herein, its answers to paragraphs 1 through 45 of the Complaint.

47. Aegis is without knowledge or information sufficient to form a belief as to the truth of the allegations of paragraph 47 of the Complaint.

48. Denied.

49. Denied.

50. Denied.

51. Denied.

COUNT V
Fraudulent Misrepresentation

52. Aegis incorporates by reference, as if fully set forth herein, its answers to paragraphs 1 through 51 of the Complaint.

53. Denied.

54. Denied.

55. Denied.

56. Denied.

57. Denied.

58. Denied.

COUNT VI
False Marking

59. Aegis incorporates by reference, as if fully set forth herein, its answers to paragraphs 1 through 58 of the Complaint.

60. Denied.

61. Exhibit D, referenced in paragraph 61 of the Complaint, speaks for itself.

62. Exhibit E, referenced in paragraph 62 of the Complaint, speaks for itself.

63. Exhibit F, referenced in paragraph 63 of the Complaint, speaks for itself. The remaining factual assertions contained in paragraph 63 of the Complaint are denied.

64. Denied.

65. Denied.

Aegis denies each and every allegation contained in the Complaint that has not been specifically admitted herein. Aegis further denies that Ameritox and UDT are entitled to any of the relief sought in the Complaint and prays that all such claims be dismissed with prejudice.

AFFIRMATIVE DEFENSES

1. Aegis does not infringe, either literally or under the doctrine of equivalents, any valid and enforceable claim of the '788 Patent or of the '136 Patent.

2. The doctrine of prosecution history estoppel precludes reliance by Plaintiffs upon the doctrine of equivalents.

3. Claims of the '788 Patent and of the '136 Patent are invalid for failure to satisfy the requirements of 35 U.S.C. §§ 101, 102, 103, and/or 112.

4. Discovery and further investigations may demonstrate that the '788 Patent and/or the '136 Patent are unenforceable.

5. Plaintiffs' claims are barred under the Doctrine of Unclean Hands.

6. Plaintiffs' claims are barred to the extent Plaintiffs' lack standing.

7. The Complaint fails to state a claim upon which relief can be granted.

8. Plaintiffs' claims are barred under the Doctrine of Patent Misuse.

9. Aegis reserves the right to amend its answer to assert additional affirmative defenses upon further investigation and discovery herein.

COUNTERCLAIMS

Pursuant to Rule 13 of the Federal Rules of Civil Procedure, Aegis asserts the following counterclaims against Ameritox and UDT:

1. Aegis is a Tennessee corporation with its principal place of business at 345 Hill Avenue, Nashville, Tennessee 37210.

2. On information and belief, Counter Defendant, Ameritox, is a Texas limited partnership with its principal place of business at 3510 North A Street, Building B, Suite 200, Midland, Texas 79705.

3. On information and belief, Counter Defendant, UDT, is a Florida corporation with its principal place of business at 950 North Collier Boulevard, Suite 207, Marco Island, Florida 34145.

JURISDICTION AND VENUE

4. This Court has jurisdiction under 28 U.S.C. §§ 1331, 1332(a), 1338, 1367, 2201 and 2202. Venue in this district exists under 28 U.S.C. §§ 1391 and 1400.

FACTS

5. Aegis repeats and realleges all the averments contained in its Answer and Affirmative Defenses and incorporates them herein by reference as if set forth verbatim.

6. Aegis and Ameritox are direct competitors in the drug testing industry.

7. On information and belief, Ameritox attempts to provide a therapeutic drug monitoring service based on the results of urine drug testing, as more fully described by the claims in the Patents in Suit. However, the processes described in the Patents in Suit are only scientifically validated and recognized for testing blood and serum - not urine – and then only for certain drugs, excluding most pain management drugs. As applied to urine drug testing, the Ameritox methods as claimed in the Patents in Suit are junk science.

8. In performing its drug testing services, Aegis uses a substantially dissimilar scientifically validated and recognized method.

9. In an effort to gain an unfair, improper and unlawful advantage in its competition with Aegis in the marketplace, Ameritox has engaged in a concerted effort to disparage, and harm the reputation of Aegis. Additionally, Ameritox and UDT have initiated and maintained this objectively baseless "sham litigation" against its competitor, Aegis, without regard to the merits of the litigation, in order to exploit the judicial processes (as opposed to the outcome of the process) as an anticompetitive weapon.

10. In these endeavors, in connection with the promotion of its services, Ameritox has willfully made false and/or misleading representations of fact regarding the nature and qualities

of the services and commercial activities of Aegis, including false accusations of unethical and unlawful conduct, false and misleading statements regarding the drug testing services provided by Aegis, and the false accusation that Aegis uses the same junk science employed by Ameritox in providing its drug monitoring services.

11. Specifically, among other false and misleading representations made, Ameritox and its agents, employees and/or sales representatives have stated to clients and prospective clients of Aegis that: "They [Aegis] copied us;" "They [Aegis] stole our business model;" Aegis is "doing what we [Ameritox] are doing, but not as well and we give you much more usable information;" "Aegis is not giving enough information in their report;" and "Aegis doesn't do what the Physician needs. We [Ameritox] give you information that can tell whether or not your patient is really compliant."

12. As a result of Ameritox' numerous false, and sometimes contradictory, representations about Aegis in the marketplace, and the filing and continued pursuit of this sham litigation, Aegis has been and will likely continue to be damaged.

COUNT ONE
(Non-infringement of the '788 Patent)

13. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

14. UDT claims to be the assignee and owner and Ameritox claims to be the exclusive licensee of the '788 Patent.

15. There is an actual, substantial and continuing justiciable controversy between Ameritox, UDT and Aegis regarding the infringement, validity and enforceability of the '788 Patent.

16. Aegis has not infringed any valid and enforceable claim of the '788 Patent.

17. Aegis is entitled to a declaration that it does not infringe any valid and enforceable claim of the '788 Patent.

COUNT TWO
(Invalidity of the '788 Patent)

18. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

19. The claims of the '788 Patent are invalid for failure to satisfy the statutory requirements for patentability of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103 and/or 112.

20. Aegis is entitled to a declaration that all claims of the '788 Patent are invalid.

COUNT THREE
(Non-Infringement of the '136 Patent)

21. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

22. UDT claims to be the assignee and owner and Ameritox claims to be the exclusive licensee of the '136 Patent.

23. There is an actual, substantial and continuing justiciable controversy between Ameritox, UDT and Aegis regarding the infringement, validity and enforceability of the '136 Patent.

24. Aegis has not infringed any valid and enforceable claim of the '136 Patent.

25. Aegis is entitled to a declaration that it does not infringe any valid and enforceable claim of the '136 Patent.

COUNT FOUR
(Invalidity of the '136 Patent)

26. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

27. The claims of the '136 Patent are invalid for failure to satisfy the statutory requirements for patentability of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103 and/or 112.

28. Aegis is entitled to a declaration that all claims of the '136 Patent are invalid.

COUNT FIVE
(Commercial Disparagement Under the Lanham Act, 15 U.S.C. § 1125(a))

29. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

30. Ameritox' false and/or misleading representations of fact regarding the nature and qualities of the services and commercial activities of Aegis, has damaged and is likely to further damage Aegis in the marketplace and constitutes commercial disparagement under the Lanham Act, 15 U.S.C. § 1125(a) entitling Aegis to an injunction, corrective advertising, treble its damages, Ameritox' profits derived from its unlawful acts, and increased pursuant to the principles of equity pursuant to the provisions of 15 U.S.C. §§ 1116 and 1117.

31. Ameritox' intentional, deliberate and willful acts constitute a willful violation of 15 U.S.C. § 1125(a) and renders this case exceptional, entitling Aegis to an award of its attorneys' fees pursuant to 15 U.S.C. § 1117.

COUNT SIX
(Unfair Competition)

32. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

33. Ameritox' concerted effort to disparage, and harm the reputation of Aegis by willfully making false and/or misleading representations of fact regarding the nature and qualities of the services and commercial activities of Aegis constitutes unfair competition under the law of the State of Florida, entitling Aegis to all remedies available under Florida law for such unfair competition.

COUNT SEVEN
(Violation of Florida Deceptive and Unfair Trade Practices Act)

34. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

35. Ameritox' concerted effort to disparage, and harm the reputation of Aegis by willfully making false and/or misleading representations of fact regarding the nature and qualities of the services and commercial activities of Aegis constitutes a violation of the Florida Deceptive and Unfair Trade Practices Act, entitling Aegis to all remedies available under such Act.

COUNT EIGHT
(Sherman Anti-Trust Act, 15 U.S.C. § 2, Sham-Litigation)

36. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

37. Ameritox and UDT have initiated and maintained this objectively baseless "sham litigation" against its competitor, Aegis, without regard to the merits of the litigation, in order to exploit the judicial processes (as opposed to the outcome of the process) as an anticompetitive weapon.

38. Ameritox and UDT's attempt to interfere with the business relationships of a competitor in this way is in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2.

39. Aegis has been injured by reason of Ameritox and UDT's antitrust violation.

COUNT NINE
(Patent Misuse)

40. Aegis repeats and realleges all the averments contained in the preceding paragraphs of its Counterclaim and incorporates them herein by reference as if set forth verbatim.

41. There is an actual, substantial and continuing justiciable controversy between Ameritox, UDT and Aegis regarding the infringement and enforceability of the Patents in Suit.

42. Aegis is entitled to a declaration that the Patents in Suit are void and unenforceable because of Ameritox's patent misuse in commencing litigation against Aegis without undertaking the necessary objective pre-filing investigation to determine whether the accused products or services infringed the claims of the Patents in Suit and then continuing this litigation knowing that Aegis did not infringe the claims of the Patents in Suit.

REQUEST FOR RELIEF

WHEREFORE, Aegis requests that judgment be entered against Ameritox and UDT:

A. Dismissing the Complaint with prejudice and denying each request for relief that Ameritox and UDT have made;

B. Declaring that Aegis does not infringe any claim of United States Patent No. 5,908,788;

C. Declaring that United States Patent No. 5,908,788, and all claims thereof, are invalid;

D. Declaring that Aegis does not infringe any claim of United States Patent No. 6,124,136;

E. Declaring that United States Patent No. 6,124,136, and all claims thereof, are invalid;

F. Declaring this case exceptional and awarding Aegis its reasonable attorneys' fees and costs under 35 U.S.C. § 285, and/or awarding Aegis its reasonable attorneys' fees and costs incurred in connection with this action pursuant to 15 U.S.C. § 15(a);

G. Declaring that Ameritox and UDT has attempted to enforce the Patents in Suit in bad faith under the Patent Misuse Doctrine and through "sham litigation" that is not premised upon any objective basis for believing the Patents in Suit had been infringed, and thus with an intent to monopolize in violation of Section 2 of the Sherman Act under Hangards, Inc. v. Ethicon, Inc., entitling Aegis to treble damages;

H. That Ameritox and its officers, directors, agents, servants, employees, and all persons in active concert and participation with it, be preliminarily and permanently enjoined

from making false and disparaging representations about Aegis and the nature and qualities of its services and commercial activities;

I. That in accordance with the Lanham Act and applicable Florida statutory and common law and as against Ameritox, awarding Aegis treble its damages, Ameritox' profits derived from its unlawful acts, and increased pursuant to the principles of equity, corrective advertising, and Aegis' costs of suit and reasonable attorneys' fees.

J. That in accordance with the Sherman Anti-Trust Act, 15 U.S.C. § 2, awarding Aegis three (3) times its damages, consisting of, among other items, all profits it could have made but for the antitrust violation, as well as all of its costs and attorneys' fees incurred in defending against this lawsuit;

K. Awarding Aegis such other and further relief as the Court deems just and proper.

Respectfully submitted,

/s/ Joel T. Galanter
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Facsimile: (954) 713-0976

Attorneys for Aegis Sciences Corp.

CERTIFICATE OF SERVICE

I hereby certify that on February 8, 2008, I electronically filed the foregoing document with the Clerk or the Court using CM/ECF. I also certify that the foregoing document is being served on all counsel of record on the below Service List in the manner specified, either via transmission of Notices of Electronic Filing generated by CM/ECF or in some other authorized manner for those counsel or parties who are not authorized to receive electronically Notices of Electronic Filing.

By:/s/ Peter R. Goldman
Peter R. Goldman
Fla. Bar No.: 860565

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EXHIBIT D

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA
WEST PALM BEACH DIVISION

AMERITOX, LTD., and U.D. TESTING, INC.	)	
Plaintiffs,	)	
v.	)	Civil Action No. 07-80498-cv-MARRA
AEGIS SCIENCES CORP.,	)	
Defendant.	)	

PLAINTIFFS' MOTION FOR LEAVE TO FILE SECOND AMENDED COMPLAINT

Plaintiffs, Ameritox Ltd. ("Ameritox") and U.D. Testing, Inc. ("UDT") (collectively "Plaintiffs") respectfully move for leave to file a Second Amended Complaint. Through this motion, Plaintiffs seek to narrow the scope of the litigation as this case moves forward. Specifically, Plaintiffs seek to dismiss their claims of patent infringement without prejudice and grant Aegis a covenant-not-to-sue for patent infringement based on the present embodiment of its PainComp™ Compliance Testing Services. In addition, Plaintiffs seek leave to add a single claim for false advertising under the Lanham Act. A copy of the proposed Second Amended Complaint is attached as **Exhibit 1** pursuant to S.D. Fla. L.R. 15.1.

Pursuant to the Local Rules of this Court, Plaintiffs conferred with opposing counsel. However, the parties could not reach agreement. In support of this motion, Plaintiffs state as follows:

BACKGROUND

Ameritox is a national leader in pain prescription monitoring and the exclusive licensee of United States Patent Nos. 5,908,788 and 6,124,136 (the "patents-in-suit").[1] The patents-in-suit relate to methods for monitoring a patient's compliance with his or her prescription drug regimen. Unlike traditional drug-testing services, which merely identify the concentration of a particular drug (or its metabolite) in a patient's urine, Ameritox' RxGuardian Pain Prescription Monitoring program ("RxGuardian") uses a patented method to quantify lab results according to a patient's demographics (height, weight) and individual dosage plan. The difference between knowing that a particular drug is present in a patient's system and knowing that the tested drug levels are consistent with a patient's prescribed dosage rate and demographics is critical to "therapeutic drug monitoring."

On June 11, 2007, Plaintiffs sued Aegis for infringement of the patents-in-suit. (Dkt. No. 1). Aegis markets, offers, and sells "pain management compliance monitoring" under the name Aegis PainComp™ Compliance Testing Services ("PainComp™"). Aegis' website and marketing materials convey that PainComp™ is ***more*** than traditional urine drug testing. For example, Aegis' website promises that PainComp™ will help physicians answer the "critical" question: ***Are your patients properly taking the medications you are prescribing?*** (See Exhibit B (emphasis in original).)[2] Likewise, Aegis' website and advertising materials stress that PainComp™ is "a valuable tool" in helping the Pain Management physician determine if his or her patients are "compliant or non-compliant" with their pain medication regimen:

---

[1] Because Plaintiffs seek to dismiss their claims of patent infringement and grant Aegis a covenant-not-to-sue, UDT is no longer a necessary party to this litigation.

[2] Exhibits A-K are attached to Plaintiffs' proposed Second Amended Complaint.

> **Compliant or Non-Compliant?**
>
> Aegis PainComp™ Testing Services are a valuable tool in helping the Pain Management Physician determine if patients are **compliant or non-compliant** with prescribed pain medications. (*Id.* (emphasis in original).)
>
> **Compliant or Non-Compliant?**
>
> The easy to read, easy to interpret PainComp™ reports will clearly show if testing indicates a patient is compliant or noncompliant with their pain medication regimen. (Exhibit A (emphasis in original).)

After analyzing and comparing Aegis' public statements, its marketing materials, and a lab report to claims of the '136 and '788 patents, Plaintiffs reasonably concluded that PainComp™ infringed the patents-in-suit and this lawsuit commenced.

The deadline to file amended pleadings was December 21, 2007. On that day, Plaintiffs filed a Motion for Leave to amend their original complaint to include four additional counts: Florida Deceptive and Unfair Trade Practices Act; Tortious Interference with Business Relationships; Fraudulent Misrepresentation; and False Marking. (Dkt. No. 24.) The Court granted Plaintiffs' motion on January 25, 2008. (Dkt. No. 28.)

After the deadline passed, however, Plaintiffs learned that Aegis' website and marketing materials misrepresent the qualities and characteristics of PainComp™. On January 11, 2008, Aegis ***admitted*** that it performs traditional drug testing and that it does not consider drug dosage prescribed by a physician. (Exhibit E at ¶ 5.) On April 7, 2008, Aegis ***admitted*** that it does not "associate the urine drug concentration to the dose of drug used by the doctor." (Exhibit F at ¶ 8.) Moreover, Ameritox technical, management and legal representatives visited Aegis' Nashville, Tennessee facility on March 20, 2008. There, Aegis explained its testing methodology and procedures for the ***first time in this case*** as no discovery regarding PainComp™ had previously been produced. Aegis provided representative requisition forms

and other documentation that confirmed the information Aegis obtains from the physician prior to testing a urine sample. Aegis also walked Ameritox personnel and counsel through its laboratories and facility.

In light of Aegis' admissions, and the information exchanged at the March 20, 2008 meeting, Plaintiffs conducted the necessary investigation to prepare the Second Amended Complaint. Approximately one month after visiting Aegis' facility, on April 24, 2008, counsel for Plaintiffs informed Aegis that it was dismissing its infringement claims and intended to raise a claim for false advertising under the Lanham Act. On April 30, 2008, counsel for Plaintiffs forwarded a draft of the proposed Second Amended Complaint to Aegis for its review and consideration. On May 5, 2008, counsel for Plaintiffs informed Aegis that they would grant Aegis a covenant-not-to-sue. Nevertheless, Aegis objected to the proposed amendments.

Based on the foregoing, Plaintiffs seek to dismiss their infringement claims without prejudice and grant Aegis a covenant-not-to-sue for infringement of the patents-in-suit based on the present embodiment of PainComp™. **Exhibit 2**, Covenant Not to Sue dated May 8, 2008. However, Aegis' current position and admissions render past and present statements (made on its website and in PainComp™ marketing materials) false advertising under the Lanham Act, 15 U.S.C. §§ 1114-27. Accordingly, Plaintiffs move under Federal Rules of Civil Procedure 15(a) and 16(b) for leave to amend its complaint to: (1) dismiss Counts I and II for patent infringement without prejudice; and (2) add a claim for false advertising.

LAW AND ARGUMENT

The Scheduling Order set December 21, 2007 as the deadline to amend the pleadings and/or add parties. (Dkt. No. 20. at 2.) When a party moves to amend the pleadings after the time prescribed by the scheduling order, he or she must first demonstrate "good cause" under

Federal Rule of Civil Procedure 16(b). *See Sosa v. Airprint Sys, Inc.* 133 F.3d 1417, 1418 (11th Cir. 1998); *Donahay v. Palm Beach Tours & Trans., Inc.*, 243 F.R.D. 697, 699 (S.D. Fla. 2007). "[G]ood cause exists when evidence supporting the proposed amendment would not have been discovered in the exercise of reasonable diligence until after the amendment deadline has passed." *Donahay*, 243 F.R.D. at 699 (citing *Forstmann v. Culp,* 114 F.R.D. 83, 85-86 (M.D.N.C.1987)).

If "good cause" is shown, the moving party must demonstrate that the amendment is proper under Federal Rule of Civil Procedure 15(a). In determining whether leave to amend is appropriate under Rule 15(a), the courts analyze the presence of the following factors: bad faith, undue delay, prejudice to the opposing party, and/or futility. *Foman v. Davis*, 371 U.S. 178, 182 (1962); *see also Brewer-Giorgio v. Producers Video, Inc.*, 216 F.3d 1281, 1284 (11th Cir. 2000) (citations omitted). "[U]nless a substantial reason exists to deny leave to amend, the discretion of the District Court is not broad enough to permit denial." *Florida Evergreen Foliage v. E.I. DuPont De Nemours & Co.*, 470 F.3d 1036, 1041 (11th Cir. 2006) (quoting *Shipner v. E. Air Lines, Inc.,* 868 F.2d 401, 407 (11th Cir. 1989)).

A. "Good Cause" Exists Under Federal Rule of Civil Procedure 16(b)

1. Plaintiffs Recently Learned the Facts Necessary to Support its Claim for False Advertising

"The fact that a party first learns, through discovery or disclosure, information necessary for the assertion of a claim after the deadline to amend established in the scheduling order has expired constitutes good cause to extend that deadline." *Pumpco, Inc. v. Schenker Int'l Inc.*, 204 F.R.D. 667, 668-9 (D. Colo. 2001). Here, Plaintiffs did not have sufficient knowledge of the facts relevant to the proposed amendment until April 7, 2008—almost four months ***after*** the December 21, 2007 deadline passed. Under these circumstances, courts routinely find that "good

cause" exists to extend a scheduling order. *Id.* (granting the plaintiff's motion to amend its complaint based on information discovered after the deadline passed); *Navarro v. Eskanos & Adler*, 2006 WL 3533039 (N.D. Cal. Dec. 7, 2006) (same); *Permasteelisa CS Corp. v. Airolite Co., LLC*, 2007 WL 1683668 (S.D. Ohio June 8, 2007) (same).

Plaintiffs had no reason to believe that PainComp™ did not include the advertised features: (i) when it filed this lawsuit, or (ii) on December 21, 2007, the deadline for amending the pleadings. Aegis' website promised that PainComp™ can assist the Pain Management Physician in answering the "critical" question: Are your patients properly taking the medications you are prescribing? *Id.* Aegis' website and advertising materials further characterized PainComp™ as "a valuable tool" in helping the Pain Management physician determine if his patients are "compliant or non-compliant" with their pain medication regimen.

Aegis did not admit that it performs "traditional drug testing" until ***after*** the deadline to amend the pleadings passed. On January 11, 2008, Aegis opposed Plaintiffs' motion to file a First Amended Complaint and attached the Declaration of Aegis' CEO Dr. David L. Black in support. Dr. Black admitted:

- "Aegis performs what is commonly considered by medical professionals to be traditional urine drug testing . . ."
- "In performing its service, Aegis does not consider the amount of drug prescribed by the physician."

(Exhibit E, ¶ 5.) In contrast, therapeutic drug monitoring (like Ameritox' RxGuardian) tests "drug levels based upon prescribed dosage to evaluate if a patient has too much or too little in their body." *Id.*

In early February 2008, the parties initiated settlement discussions in a good-faith effort to resolve the issues in this case. While no settlement was reached, Aegis subsequently offered to have Plaintiffs inspect its laboratory and facilities. The parties agreed to meet in Nashville, Tennessee on March 20, 2008.

It was during this meeting that Plaintiffs ***first learned*** Aegis' non-infringement positions. Although Plaintiffs previously requested that Aegis disclose its non-infringement position in response to discovery, Aegis failed to provide substantive responses. Instead, at the March meeting, it provided documentation, including representative requisition forms, which confirmed the information Aegis obtains from the physician prior to testing a urine sample. In addition, it walked Plaintiffs' representatives through its facilities to analyze the procedures used by Aegis.

Finally, on April 7, 2008, Aegis responded to Plaintiffs' Motion to Dismiss its counterclaim for sham litigation and patent misuse. Aegis attached a second declaration from Dr. Black in support. At that time, Dr. Black admitted that Aegis does not "associate the urine drug concentration to the dose of drug used by the donor." (Exhibit F, at ¶ 8.)

2. Plaintiffs' Motion Is Timely and Made In Good Faith

In light of Aegis' admissions, and the information exchanged at the March 20, 2008 meeting, Plaintiffs diligently conducted the necessary investigation to prepare a Second Amended Complaint, including a technical analysis of Aegis' non-infringement positions against the asserted claims of the patents-in-suit. On April 24, 2008—approximately one month after the parties' meeting in Nashville, Tennessee—counsel for Plaintiffs informed Aegis that it was dismissing its infringement claims and intended to raise a claim for false advertising under the Lanham Act. *See Weiss v. PPG Indus., Inc.*, 148 F.R.D. 289, 292 (M.D. Fla. 1993) ("The Court does not consider thirty two days to be 'undue delay' which requires the Court to deny leave to

amend.") On April 30, 2008, counsel for Plaintiffs forwarded a draft of the proposed Second Amended Complaint to Aegis for its review and consideration. On May 5, 2008, counsel for Plaintiffs informed Aegis that they would grant a covenant-not-to-sue. Nevertheless, Aegis objected to the proposed amendments.

B. Leave to Amend Is Appropriate Under Federal Rule of Civil Procedure 15(a)

1. Allowing Plaintiffs to File the Second Amended Complaint Will Not Unduly Prejudice Aegis

Plaintiffs' Second Amended Complaint will not unduly prejudice Aegis or greatly expand the nature of this lawsuit. In early February 2008, the parties initiated settlement discussions, which continued on a regular basis through April. As a result, discovery is in its preliminary stages. No depositions have taken place to date. No dispositive motions have been filed. Indeed, on May 2, 2008, Aegis served its First Supplemental Responses to Plaintiffs' Interrogatories and Document Requests, producing documents for the first time in this case.

Moreover, the proposed false advertising claim relates to public statements and advertisements concerning PainComp™ and "thereby complements the discovery engaged in by the parties to date." *Transwitch Corp. v. Galazar Networks, Inc.*, 377 F. Supp. 2d 284, 292 (D. Mass. 2005) (granting the plaintiff's motion to dismiss its patent infringement claims and add a claim for false advertising). For example, Document Request No. 14 seeks all documents that Aegis distributed at conferences, demonstrations, or sales shows regarding its "pain medication compliance testing services." Similarly, Document Request No. 15 seeks advertising, promotional, and marketing materials offered or provided in connection with PainComp™.

In addition, all of Aegis' discovery requests to date have only involved patent infringement and invalidity. Aegis has not served Plaintiffs with discovery requesting information related to Plaintiffs' claims of Florida Deceptive and Unfair Trade Practices Act,

Tortious Interference with Business Relationships, Fraudulent Misrepresentation, or False Marking—all of which have been pending since January 25, 2008.

2. Plaintiffs' Second Amended Complaint States a Claim for False Advertising

Leave to amend a complaint is only futile "when the complaint as amended would still be properly dismissed or be immediately subject to summary judgment for the defendant." *Cockrell v. Sparks*, 2007 WL 4439739, *2 (11th Cir. 2007) (citing *Hall v. United Ins. Co. of Am.*, 367 F.3d 1255, 1263 (11th Cir. 2004). "The elements of a claim under the Lanham Act for false advertising are: (1) the ads of the opposing party were false or misleading, (2) the ads deceived, or had the capacity to deceive, consumers, (3) the deception had a material effect on purchasing decisions, (4) the misrepresented product or service affects interstate commerce, and (5) the movant has been-or is likely to be-injured as a result of the false advertising." *Air Turbine Technology, Inc. v. Atlas Copco AB*, 295 F. Supp. 2d 1334, 1343 (S.D. Fla. 2003) (quoting *Johnson & Johnson Vision Care, Inc. v. 1-800 Contacts, Inc.*, 299 F.3d 1242, 1247 (11th Cir. 2002). Plaintiffs' proposed Second Amended Complaint includes at least the following allegations:

> 16. Aegis' website, advertising materials, and sample lab reports characterize PainComp™ as a tool for its clients to determine if their patients are complying with their prescribed drug regimens.
>
> 17. Aegis' website describes PainComp™ as "Pain Medication Compliance Testing Services." It further states that PainComp™ is designed "to assist the Pain Management Physician in answering two critical questions concerning patient use of medications: 1. Are your patients properly taking the medications you are prescribing? 2. Are your patients taking other drugs that may interfere with the medications you are prescribing?" The website also reiterates, "Aegis PainComp™ Testing Services are a valuable tool in helping the Pain Management physician determine if patients are compliant or non-compliant with prescribed pain medications."

18. Aegis' advertising materials likewise characterize PainComp™ as "a valuable tool in helping you determine if your patients are compliant with the medications you are prescribing." In addition, the advertising materials state that Aegis' "easy to read, easy to interpret PainComp™ reports will clearly show if testing indicates a patient is compliant or noncompliant with their pain medication regimen."

20. Upon information and belief, Aegis falsely advertises and/or misrepresents the nature, characteristics, and qualities of PainComp™ to consumers; including false and misleading statements that PainComp™ measures a patient's compliance "with their pain medication regimen" and is "a valuable tool in helping the Pain Management physician determine if patients are compliant or non-compliant with prescribed pain medications."

23. Based on Aegis' website, advertising materials, and sample lab reports, a pain management physician using PainComp™ can determine if a ***particular*** patient "is compliant or noncompliant with their pain medication regimen."

24. But, Aegis ***admits*** that PainComp™ only determines the amount of a substance found in the patient's urine. Aegis does not take into consideration the drug regimen and medication dosage prescribed by a doctor.

30. Furthermore, upon information and belief, Aegis does not take into consideration specific patient demographics, including height and weight. For example, Aegis' Laboratory Request form (i.e., requisition form) asks for none of the patient's physical characteristics other than gender and age.

45. Aegis' statements are literally false and/or likely to deceive customers about the true nature, characteristics, and qualities of its PainComp™ services.

> 46. Aegis' false or misleading statements have already, and will continue, to influence purchasing decisions to the extent that customers choose Aegis' services instead of those offered by Ameritox.
> 47. PainComp™ is offered, advertised, and sold to customers throughout the country; therefore, the misrepresented services affect interstate commerce.
>
> 48. As a direct and proximate result of Aegis' conduct, Ameritox has incurred actual damages and is entitled to all remedies available under the law.

(citations omitted).

The Second Amended Complaint properly alleges the elements of a claim for false advertising under the Lanham Act. Further, all of Plaintiffs' claims are properly supported by the facts that it uncovered through their investigation of Aegis' conduct, including Aegis' own admissions. As a result, the proposed amendment is not futile and Plaintiffs respectfully request that the Court grant them leave to file the Second Amended Complaint.

Conclusion

WHEREFORE, Plaintiffs respectfully request that they be granted leave to file their Second Amended Complaint.

CERTIFICATE OF GOOD FAITH EFFORT PURSUANT TO RULE 7.1

Undersigned Counsel for Plaintiffs, Ameritox and UDT, hereby certify pursuant to S.D. Fla. L.R. 7.1 that he has conferred with counsel for Aegis in a good faith effort to resolve the issues raised in this motion and has been unable to do so.

Dated: May 8, 2008

By: /s/ Michael R. Osterhoff
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CERTIFICATE OF SERVICE

I hereby certify that on May 8, 2008, I electronically filed the foregoing document with the Clerk or the Court using CM/ECF. I also certify that the foregoing document is being served on all counsel of record on the below Service List in the manner specified, either via transmission of Notices of Electronic Filing generated by CM/ECF or in some other authorized manner for those counsel or parties who are not authorized to receive electronically Notices of Electronic Filing.

/S/: Christopher P. Demetriades
Christopher P. Demetriades, Esq.

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SERVICE LIST
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Case No. 07-80498
United States District Court, Southern District of Florida

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EXHIBIT E

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA
WEST PALM BEACH DIVISION

AMERITOX, LTD., and U.D. TESTING, INC.,	)	
Plaintiffs,	)	Case No. 07-80498-MARRA/JOHNSON
v.	)	
AEGIS SCIENCES CORP.,	)	
Defendant.	)	

MOTION TO DISMISS AEGIS' SHERMAN ANTI-TRUST ACT SHAM LITIGATION AND PATENT MISUSE CLAIMS

Plaintiffs Ameritox, Ltd. ("Ameritox") and U.D. Testing, Inc. ("UDT") (collectively, "Plaintiffs") respectfully move to dismiss Defendant Aegis Sciences Corp.'s ("Aegis") Sherman Anti-trust Act Sham Litigation and Patent Misuse Claims under Rule 12(b)(6) of the Federal Rules of Civil Procedure. The grounds supporting this Motion are as follows:

Introduction

Defendant's Amended Answer and Counterclaim allege facts that, even if true, cannot support its new contentions for Sherman Anti-trust Act Sham Litigation and Patent Misuse Claims. First, Defendant's alleged facts for sham litigation and patent misuse are simply labels, conclusions, and formulaic recitations of the elements of the causes of action with no factual underlying bases. Second, even if true, Defendant's alleged facts for sham litigation cannot show "the lawsuit [is] objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits," as required. Third, even if Defendant could show objective baselessness, it cannot show that Plaintiffs brought the allegedly baseless suit with a "subjective motivation ... to interfere *directly* with the business relationships of a competitor," as

is also required. Finally, Defendant's patent misuse claim fails. None of Defendant's facts, even if true, sufficiently plead a patent misuse claim. Accordingly, Defendant's Sherman Anti-trust Act Sham Litigation and Patent Misuse counterclaims must be dismissed for failure to state a claim for which relief may be granted.

Background and Procedural History

Ameritox is a Texas limited partnership and UDT is a Florida corporation. (Amended Complaint, Exhibit A, Dkt. No. 24, ¶¶ 1-2). Defendant Aegis is a Tennessee corporation. (Amended Complaint, Dkt. No. 24, ¶ 3 and Aegis' Answer to First Amended Complaint and Counterclaim, Dkt. No. 30, Answer ¶ 3[1]). UDT owns U.S. Patent Nos. 5,908,788 ("'788 Patent") and 6,124,136 ("'136 Patent") (collectively, "Patents in Suit"). (Amended Complaint, Dkt. No. 24, ¶¶ 7-8). In March of 2005, Ameritox became the exclusive licensee of the Patents in Suit. *Id.* at ¶ 9.

On June 11, 2007, Plaintiffs filed an action alleging Aegis infringes the Patents in Suit. (Complaint, Dkt. No. 1). On July 31, 2007, Aegis answered the Complaint and filed Counterclaims alleging non-infringement and invalidity of the '788 and '136 Patents, Commercial Disparagement under the Lanham Act, Injurious Falsehood/Unfair Competition, and a Violation of the Florida Deceptive and Unfair Trade Practices Act. (Aegis' Answer and Counterclaims, Dkt. No. 15).

On December 21, 2007, Plaintiffs filed a Motion for Leave to Amend their Complaint along with their proposed Amended Complaint with four additional Counts: Florida Deceptive and Unfair Trade Practices Act; Tortious Interference with Business Relationships; Fraudulent Misrepresentation; and False Marking. (Amended Complaint, Exhibit A, Dkt. No. 24). Aegis

[1] Plaintiffs use "Answer ¶" when referring to Aegis' Answer portion of its Answer to First Amended Complaint and Counterclaim and "Counterclaim ¶" when referring to Aegis' Counterclaim portion.

vigorously opposed the amendment. (Order, Dkt. No. 28 and Aegis' Response to Motion to Amend, Dkt. No. 26).

On January 25, 2008, this Court granted Plaintiffs' Motion for Leave and entered their Amended Complaint. (Order, Dkt. No. 28 and Amended Complaint, Exhibit A, Dkt. No. 24). On February 8, 2008, Aegis filed its Amended Answer and Counterclaims adding two additional counterclaims for Sherman Anti-Trust Act Sham Litigation and Patent Misuse. (Aegis' Answer to First Amended Complaint and Counterclaim, Dkt. No. 30). These counterclaims are the subject of the instant Motion.

Argument

It is well settled that a claim should be dismissed for failure to state a claim when "it appears beyond a doubt that the [counterclaimant] could prove no set of facts in support of his claim which would entitle him to relief." *Conley v. Gibson,* 355 U.S. 41 (1957); *see also Linder v. Portocarrero*, 963 F.2d 332, 334 (11th Cir. 1992); *Apex Mach. Co. v. Ritter GmbH*, 2007 WL 601719, *1 (S.D. Fla. Feb. 16, 2007). Recently, the Supreme Court clarified this standard. *Bell Atlantic Corp. v. Twombly,* 127 S.Ct. 1955 (2007). Pursuant to *Bell Atlantic,* counterclaims should be dismissed when they contain factual allegations that fail "to raise a right to relief above the speculative level." 127 S.Ct. at 1965. As under *Conley,* a complaint must be liberally construed, assuming the facts alleged therein as true and drawing all reasonable inferences from those facts in the plaintiff's (or counterclaim-plaintiff's) favor. *Id.* at 1964-65; *see also Apex Mach. Co.*, 2007 WL 601719 at *1 (citing *Cramer v. Florida,* 117 F.3d 1258, 1262 n. 8 (11th Cir. 1997) ("The allegations of the claims in question must be taken as true and must be read to include any theory on which the plaintiff may recover."); *Linder v. Portocarrero,* 963 F.2d at 334-36. However, a court "is not bound to accept as true a legal conclusion couched as a factual

allegation." *Id.* at 1965 (citing *Papasan v. Allain*, 478 U.S. 265, 286 (1986)). Certainly, "[w]hile a complaint attacked by a Rule 12(b)(6) motion to dismiss does not need detailed factual allegations, a plaintiff's obligation to provide the 'grounds' of his 'entitle[ment] to relief' requires more than labels and conclusions, and a formulaic recitation of the elements of a cause of action will not do." *Bell Atlantic,* 127 S.Ct. at 1964-65 (internal citations omitted).

Here, as the Supreme Court has explicitly admonished, Aegis only alleges its claims of sham litigation and patent misuse with labels, conclusions, and formulaic recitations of the elements of the causes of action with no factual underlying bases. Aegis' allegations stem from its dislike of the Plaintiffs' claims and nothing more. Accordingly, Aegis' counterclaims of sham litigation and patent misuse fail as a matter of law and should be dismissed.

I. Aegis' Counterclaim Alleging Sham Litigation Must be Dismissed for Failure to State a Claim

Under the *Noerr-Pennington* doctrine, a patent holder is immune from antitrust liability when it sues to enforce its constitutionally-granted patent rights. *Andrx Pharmaceuticals, Inc. v. Elan Corp., PLC*, 421 F.3d 1227, 1233-34 (11th Cir. 2005). The exception to the *Noerr-Pennington* immunity exists where the patent holder engages in "sham litigation." *Id.*

A party bringing a sham litigation case must establish that: (1) "the lawsuit [is] objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits"; and (2) the party bringing the allegedly baseless suit did so with a "subjective motivation ... to interfere *directly* with the business relationships of a competitor." *Andrx Pharms, Inc.*, 421 F.3d at 1234 (emphasis in original) (quoting *Professional Real Estate Investors v. Columbia Pictures Indus., Inc.,* 508 U.S. 49, 60-61 (1993)). Aegis' allegations fail to support a sham litigation claim.

Moreover, Aegis' obligation to provide the grounds for relief under *Noerr-Pennington's* sham litigation exception requires more than labels, conclusions, and a formulaic recitation of the elements of a cause of action. *Bell Atlantic,* 127 S.Ct. at 1964-65. While Rule 8 of the Federal Rules of Civil Procedure requires only a short and plain statement of the claim showing that the pleader is entitled to relief to give the defendant fair notice of, and the grounds for, those claims, it also "requires a 'showing,' rather than a blanket assertion, of entitlement to relief." *Id.* at 1965 n. 3 (stating that without factual allegations, it is difficult to satisfy the requirement of providing both "fair notice" of the nature of the claims as well as the "grounds" upon which the claims rest).

a. Aegis' Alleged Facts, Even if True, Do Not Show an Objectively Baseless Lawsuit

Aegis' use of words such as "objectively baseless," "false," and "misleading" throughout its counterclaims does not satisfy the pleading requirements. *Spanish International Communications Corp., Sin, Inc. v. Leibowitz*, 608 F. Supp. 178, 184 (S.D. Fla. 1985) (granting motion to dismiss where Plaintiffs "attempted to invoke the 'sham exception' by repeating talismanic phraseology" and "utilizing the words 'sham' thirteen times, 'false' or 'falsely' eleven times, and the phrase 'baseless and repetitive' no less than fourteen times."). Aegis merely recites the elements of a sham litigation claim and, in some instances, does so multiple times. For example, Aegis alleges Plaintiffs initiated and maintained an "objectively baseless 'sham litigation'" against Aegis, "without regard to the merits of the litigation." (Aegis' Answer to First Amended Complaint and Counterclaim, Dkt. No. 30, Counterclaim ¶¶ 9, 37). Aegis also alleges that Plaintiffs violated Section 2 of the Sherman Act and that "Aegis has been injured by reason of [Plaintiffs'] antitrust violation." *Id.* at Counterclaim ¶¶ 38-39. Moreover, Aegis' repetitive use of the word "false" in connection with the majority of its allegations amounts to

nothing more than naked allegations. *See e.g., id.* at Counterclaim ¶¶ 10-12, 30, 33, and 35; *see also Spanish Int'l Comm. Corp., Sin, Inc.,* 608 F. Supp. at 184 (stating that the naked allegations of sham pleadings "is not sufficient to withstand a motion to dismiss."). Therefore, Aegis' insufficient Sherman Act pleading should be dismissed.

Even if Aegis' alleged facts were true, Aegis cannot prove that "the lawsuit is objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits." *Andrx Pharms., Inc.,* 421 F.3d at 1233-34. Regarding this first prong of the sham litigation exception, the Supreme Court noted that a "reasonable belief that there is a chance that a claim may be held valid upon adjudication" is not objectively baseless. *See Prof'l Real Estate Investors,* 508 U.S. at 62. Here, Plaintiffs' lawsuit is not objectively baseless. Plaintiffs have a right to enforce their patents. The Patent laws are anticompetitive in nature and simply because Aegis is a competitor does not give it the right to infringe Plaintiffs' patents. Moreover, in its pleading, Aegis answers Plaintiffs' allegations regarding Aegis' false marking of its Zero Tolerance Drug Testing Program by stating the relevant exhibits speak for themselves. (Aegis' Answer to Plaintiff's First Amended Complaint, Dkt. No. 30, Counterclaim ¶¶ 61-63; Amended Complaint, Exhibit A, Dkt. No. 25 at Exhibits D, E, and F)[2]. Indeed, the exhibits show that Plaintiffs notified Aegis on August 8, 2007, of its false marking of its "patented" Zero Tolerance Drug Testing product and that Aegis acknowledged and claimed to rectify the false marking immediately. (Amended Complaint, Exhibit A, Dkt. No. 25 at Exhibits D and E). Yet, Exhibit F shows that as of December 21, 2007, Aegis continued to falsely mark its Zero Tolerance Drug Testing product with the word "patented." *Id.* at Exhibit F. This example alone demonstrates

[2] Because Aegis refers to these Exhibits in its pleading and they are central to its claim that Plaintiffs lawsuit is objectively baseless, the Court may consider the documents as part of the pleadings for purposes of a Rule 12(b)(6) dismissal. *Adamson v. Poorter*, 2007 WL 2900576 (11th Cir. 2007).

that Plaintiffs' lawsuit is not objectively baseless. 35 U.S.C. § 292 ("Whoever marks upon, or affixes to, or uses in advertising in connection with any unpatented article, the word "patent" or any word or number importing that the same is patented for the purpose of deceiving the public.").

Because Aegis cannot reasonably show that "the lawsuit is objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits," Aegis' sham litigation counterclaim should be dismissed.

b. Aegis' Alleged Facts Cannot Demonstrate that Plaintiffs' Brought Their Lawsuit With a Subjective Motivation to Interfere Directly With the Business Relationships of a Competitor.

As shown above, Aegis' alleged facts, even if true, cannot support its claim of objectively baseless sham litigation. Accordingly, the sham litigation inquiry ends there. Even if, for purposes of this Motion, Aegis' alleged facts demonstrated an objectively baseless lawsuit, Aegis' alleged facts cannot demonstrate the required element that Plaintiffs brought their "allegedly baseless suit with a subjective motivation to interfere directly with the business relationships of a competitor." *Andrx Pharms., Inc.,* 421 F.3d at 1233-34.

Concerning this second prong, Aegis again disguises its sham litigation claim with labels, conclusions, and formulaic recitations of the elements of the cause of action with no factual underlying bases. For example, Aegis alleges that Plaintiffs have initiated an objectively baseless lawsuit "in order to exploit the judicial processes (as opposed to the outcome of the process) as an anticompetitive weapon," and that Plaintiffs' "attempt to interfere with the business relationships of a competitor. . . in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2. (Aegis' Answer to Plaintiff's First Amended Complaint, Dkt. No. 30, Counterclaim ¶¶ 9, 37, and 38); *see Prof'l Real Estate Investors,* 508 U.S. at 60-61 (Regarding the second prong of the sham litigation exception, "the court should focus on whether the baseless lawsuit conceals an

attempt to interfere directly with the business relationships of a competitor through the use of the [judicial] *process* – as opposed to the *outcome* of that process – as an anticompetitive weapon.") (emphasis in original) (internal quotations omitted). Aside from reciting the element of the sham litigation claim and paraphrasing case law, Aegis' facts fail to state anything that, if taken as true, could support the contention that Plaintiffs are using this lawsuit to interfere *directly* with Aegis' business relationships. Aegis' sham litigation counterclaim must be dismissed.

II. Aegis' Counterclaim alleging Patent Misuse Must be Dismissed for Failure to State a Claim

The common acts of *per se* patent misuse include (1) tying arrangements where a patent holder conditions a patent license on the purchase of another good and (2) arrangements where the patent holder extends the term of its patent by requiring post-expiration royalties. *See e.g., Virginia Panel Corp. v. MAC Panel Co.*, 133 F.3d 860, 869 (Fed. Cir. 1997).

However, the Federal Circuit (and others) have expanded patent misuse to include practices that are neither *per se* patent misuse nor specifically excluded under 35 U.S.C. § 271(d), but expand the patent holder's rights beyond the scope of the patent. *Virginia Panel Corp.*, 133 F.3d at 869. If the practice does not broaden the scope of the patent claims, it cannot constitute patent misuse. *Id.* In contrast, if the practice extends the patent holder's statutory rights, the practice must be analyzed under the "rule of reason." *Id.* Under the rule of reason, "the finder of fact must decide whether the questioned practice imposes an unreasonable restraint on competition, taking into account a variety of factors, including specific information about the relevant business, its condition before and after the restraint was imposed, and the restraint's history, nature, and effect." *State Oil Co. v. Kahn,* 522 U.S. 3, 10 (1997).

Aegis' allegations fail to support a patent misuse claim under any theory. Aegis clearly does not allege *per se* patent misuse. Aegis' allegations can not even support a patent misuse

claim under the rule of reason. In fact, Aegis' basis for patent misuse fails. Specifically, Aegis alleges that Ameritox committed patent misuse by "commencing litigation [ ] without undertaking the necessary objective pre-filing investigation to determine whether the accused products or services infringed" the patent claims and continuing "this litigation knowing that Aegis did not infringe" the patent claims. (Aegis' Answer to First Amended Complaint and Counterclaim, Dkt. No. 30, ¶ 42). Plaintiffs have been unable to find any legal support that the sufficiency of a pre-filing investigation is the proper basis of a patent misuse claim. Indeed, if Aegis has an issue with Plaintiffs' pre-filing investigation, there are proper vehicles under the Federal Rules of Civil Procedure to address the issue. Accordingly, Aegis' patent misuse claim must be dismissed.

Even if the sufficiency of a pre-filing investigation can be the basis of a patent misuse claim, Aegis' claim still fails. None of Aegis' facts, even if true, demonstrate that Plaintiffs are unlawfully expanding the scope of their patents in commencing this litigation. *See Virginia Panel,* 133 F.3d at 869. Indeed, Plaintiffs have a right to enforce their patents. *See* 35 U.S.C. § 271(d)(3) ("No patent owner otherwise entitled to relief for infringement [ ] of a patent shall be denied relief or deemed guilty of misuse or illegal extension of the patent right by reason of his having . . . sought to enforce his patent rights against infringement); *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d, 1340, 1373 (Fed. Cir. 1998) ("A patent will not be rendered unenforceable for misuse if the patent owner has enforced the patent in the good faith belief that the accused products infringed the patent's claims."). The mere fact that Aegis does not like the lawsuit or believe that it is infringing Plaintiffs' patents does not, in itself, create grounds for a patent misuse claim. To allow Aegis' patent misuse claim would essentially mean that every

patent holder that is not successful in an infringement action is guilty of patent misuse.[3] Aegis' patent misuse counterclaim should be dismissed.

Conclusion

WHEREFORE, Plaintiffs respectfully request that this Court enter an order dismissing Aegis' Sherman Anti-trust Act Sham Litigation and Patent Misuse counterclaims.

Dated: February 28, 2008

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[3] Moreover, Aegis' contention that Plaintiffs' Patents in Suit are "junk science" and not "scientifically valid" is irrelevant to a patent infringement claim, and thus, irrelevant to a patent misuse claim. *See* Aegis' Answer to First Amended Complaint and Counterclaim, Dkt. No. 30, Counterclaim ¶ 7. Indeed, if a product or process infringes all the elements of a claim in a patent, that party is liable for patent infringement regardless of "scientific validity" or "recognition." *See* 35 U.S.C. § 271.

CERTIFICATE OF SERVICE

I hereby certify that on February 28, 2008, I electronically filed the foregoing document with the Clerk or the Court using CM/ECF. I also certify that the foregoing document is being served on all counsel of record on the below Service List in the manner specified, either via transmission of Notices of Electronic Filing generated by CM/ECF or in some other authorized manner for those counsel or parties who are not authorized to receive electronically Notices of Electronic Filing.

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SERVICE LIST
Ameritox Ltd. and U.D. Testing, Inc. v. Aegis Sciences Corp.
Case No. 07-80498
United States District Court, Southern District of Florida

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IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA
WEST PALM BEACH DIVISION

AMERITOX, LTD., and U.D. TESTING, INC.,	)	
Plaintiffs,	)	
v.	)	Case No. 07-80498-MARRA/JOHNSON
AEGIS SCIENCES CORP.,	)	
Defendant.	)	

REPLY IN SUPPORT OF MOTION TO DISMISS AEGIS' SHERMAN ANTI-TRUST ACT SHAM LITIGATION AND PATENT MISUSE CLAIMS

Aegis obviously recognizes that its counterclaims for sham litigation and patent misuse are not well-pleaded. In order to fill in the blanks, Aegis introduces allegations, exhibits, and fact declarations that form no part of the official pleadings. For example, Aegis asks the Court to consider two declarations submitted months ago in opposition to Plaintiffs' Motion for Leave to file an amended complaint: "Aegis has also filed two factual declarations as exhibits to the Defendant's Response In Opposition To Plaintiff's [sic] Motion to Amend (Exhibits to Docket No. 26)." (Response at 1, 4-8).

It is well-settled that a motion to dismiss tests the sufficiency of the ***pleadings***.[1] *Henthorn v. Dept. of Navy*, 29 F.3d 682, 688 (D.D.C. 1994). In ruling on a motion to dismiss, "a court may only examine the four corners of the complaint and not matters outside the complaint without converting the motion to dismiss to a motion for summary judgment." *Caravello v. American Airlines, Inc.*, 315 F.Supp.2d 1346, 1348 (S.D. Fla. 2004). Likewise, a court should

[1] Contrary to Aegis' interpretation, fact declarations are not "pleadings" under Federal Rule of Civil Procedure 7(a). (Response at 1).

not consider allegations raised for the first time in a legal brief or memorandum. *Carswell v. Air Line Pilots Assoc., Int.*, --- F.Supp.2d ---, 2008 WL 564945, at *11 (D.D.C. Mar. 4, 2008); *Gebhart v, Allspect, Inc.*, 96 F.Supp.2d 331, 335 (S.D.N.Y. 2000).

Aegis cannot draw upon facts outside of the pleadings. Nor can it cut and paste new counterclaims from "evidence" appended to its Response. *See Carswell*, 2008 WL 564945, at *11. Thus, the ***only*** documents relevant to the instant motion are Aegis' Answer and Counterclaim and its Answer to First Amended Complaint and Counterclaim.

A. Aegis Fails to Plead Any Facts that Plaintiffs' Patent Infringement Claims Are Objectively Baseless

Aegis fails to state a claim that Plaintiffs violated Section Two of the Sherman Act. To plead attempted monopolization via sham litigation, Aegis must allege: (1) Plaintiffs engaged in predatory or anti-competitive conduct (i.e., sham litigation), (2) with the specific intent to monopolize; and (3) a dangerous probability exists that Plaintiffs will achieve monopoly power. *Securitypoint Media LLC v. The Adason Group, LLC*, 2007 WL 2298024, at *3 (M.D. Fla. Aug. 7, 2007). A single action constitutes sham litigation if "(1) the lawsuit is objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits; and (2) the party bringing the allegedly baseless lawsuit did so with a subjective motivation to interfere directly with the business relationships of a competitor." *Id.* at *4.

Courts regularly require that a party include allegations of the specific activities that give rise to liability under the Sherman Act for sham litigation. *See Spanish Int'l. Comm. Corp., SIN, Inc. v. Leibowitz*, 608 F.Supp. 178, 182 (S.D. Fla. 1985). For example, in *Catch Curve, Inc. v. Venali, Inc.*, 519 F.Supp.2d 1028 (C.D. Cal. 2007), the court held that defendant sufficiently pleaded a counterclaim for sham litigation because it alleged that the patentee relied upon an unreasonable claim construction to support its infringement claims. In *Netflix, Inc. v.*

Blockbuster, Inc., 2006 WL 2458717, at *2-3 (N.D. Cal. Aug. 22, 2006), a declaratory judgment plaintiff pleaded a counterclaim for sham litigation on the basis that the patents were invalid and overbroad. Specifically, the plaintiff alleged that the patentee (1) omitted material prior art references during prosecution of the patents in suit (the '450 patent and the '381 patent), and (2) flooded the PTO with over 100 references during prosecution of the '381 patent. The court held that the plaintiff's complaint satisfied the objective component of the sham litigation test: "If the above allegations about omitted prior-art references, flooding, and withholding prior art from the PTO examiner are proven, plaintiff may demonstrate the requisite abuse of process to succeed on a sham-litigation claim." *Id.* at *8.

As a threshold matter, Aegis fails to allege that "no reasonable litigant" could realistically expect to succeed on the merits of the asserted patent infringement claims; therefore, the counterclaim is facially defective. Furthermore, Aegis utterly fails to adduce ***any*** facts to support its unfounded claim that Plaintiffs' lawsuit is "objectively baseless." Aegis' three paragraph count for sham litigation provides in pertinent part:

> 37. Amertiox and UDT have initiated and maintained this objectively baseless "sham litigation" against its competitor, Aegis, without regard to the merit of the litigation, in order to exploit the judicial process (as opposed to the process) as an anticompetitive weapon.

Rote incantation of the phrases "objectively baseless" and "sham litigation" does not satisfy Aegis' pleading requirements. *Berry v. Budget Rent A Car Systems, Inc.*, 497 F.Supp.2d 1361, 1364 (S.D. Fla. 2007) (labels, conclusions, "and a formulaic recitation of the elements of a cause of action will not do.") (quoting *Bell Atlantic Corp. v. Twombly*, (2007) 127 S.Ct. 1955, 1964-65). At a minimum, Aegis must plead sufficient ***factual allegations*** "to raise a right to relief above the speculative level." *Id.* at 1364. Unlike the pleadings in *Catch Curve* and *Netflix*,

Aegis' counterclaim for sham litigation does not meet the minimum standard and thus should be dismissed.

B. Aegis' Patchwork Claim that Plaintiffs' Patent Infringement Claims Are Objectively Baseless Fares No Better

In an effort to piece together a sham litigation count, Aegis cherry-picks random, unrelated statements from other portions of its counterclaim. Aegis contends it properly asserted that Plaintiffs' patent infringement claims are objectively baseless because it "specifically alleges that Ameritox did not undertake the necessary objective pre-filing investigation" and "Ameritox continued this suit knowing that Aegis did not infringe the claims of the patent in suit." (Response at 4). Aegis' contentions are conclusory and untrue. Regardless, if accepted, Aegis' arguments would improperly conflate the objective and subjective prongs of the sham litigation test.

The Federal Circuit recently examined the "objectively baseless" test in the context of state and federal unfair competition claims and it rejected Aegis' arguments. In *Dominant Semiconductors SDN. BHD v. Osram GMBH*, --- F.3d ----, 2008 WL 1808336 (Fed. Cir. Apr. 23, 2008), the defendant asserted that patentee made bad faith communications to the marketplace by stating that the defendant's products infringed certain patents. The defendant claimed, among other things, that patentee's claims were "objectively baseless" and based on inadequate research:

> Dominant argues that there is no indication that Schachtner tested Dominant's products, construed the claims of any of OSRAM's patents, or considered an earlier analysis of certain Dominant products suggesting that infringement was an open question. Dominant contends that as a result, OSRAM had no reasonable basis to rely on the Schachtner letter when it made later communications to the marketplace.

Id. at *9. Affirming the district court's grant of summary judgment in patentee's favor, the Federal Circuit held that the defendant's failure to produce ***evidence that the claims were objectively baseless*** was fatal:

> ***Dominant's focus on the contention that there was no indication that Schachtner had performed a sufficient analysis, though arguably relevant on the issue subjective intent, had nothing to do with the issue of whether Schachtner's contentions were objectively baseless***

Id. at (emphasis in original and emphasis added); *see also GP Indus., Inc. v. Eran Indus., Inc.*, 500 F.3d 1369, 1375 (Fed. Cir. 2007) (holding that party's failure to obtain expert advice before alleging infringement is not a convincing objective factor).[2]

Remarkably, Aegis further contends that boiler-plate claims of non-infringement sufficiently identify the grounds upon which its claim for sham litigation rests: "Aegis has not infringed any valid and enforceable claim of the '788 Patent;" "Aegis has not infringed any valid and enforceable claim of the '136 Patent." (Response at 8; Counterclaim at ¶¶ 16, 24). The mere fact that Aegis disputes the merits of Plaintiffs' lawsuit or does not believe that it is infringing Plaintiffs' patents does not magically transform those claims into "objectively baseless." Such conclusory allegations of non-infringement, invalidity, and unenforceability are pleaded in every case and thus are insufficient to strip Plaintiffs' First Amendment right to enforce the patents-in-suit. *See e.g.*, *Argus Chemical Corp. v. Fibre Glass-Evercoat*, 812 F.2d 1381, 1386 (Fed. Cir. 1987) ("[t]he allegation by an accused infringer that the patent is invalid –

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[2] Aegis' reliance on *View Engineering, Inc. v. Robotic Vision System, Inc.*, 208 F.3d 981 (Fed. Cir. 2000), *Judin v. U.S.*, 110 F.3d 780 (Fed. Cir. 1997), and *S. Bravo Systems, Inc. v. Containment Technologies Corp.*, 96 F.3d 1372 (Fed. Cir. 1996) is misplaced. Each case dealt with a party's obligations to conduct a pre-filing investigation under Federal Rule of Civil Procedure 11. In *Dominant Semiconductors*, however, the Federal Circuit flatly rejected the defendant's attempt to equate the standard applied in Rule 11 cases with the "objectively baseless" test. 2008 WL 1808336 at *6-7.

an assertion frequently made by those charged with infringement – cannot be turned into evidence that the patentee knew the patent was invalid when it instituted an infringement suit.").

Neither Aegis' Answer and Counterclaim nor its Answer to First Amended Complaint and Counterclaim "state facts to buttress [Aegis'] naked allegation of sham pleading." *Spanish Int'l. Comm. Corp.*, 608 F.Supp. at 184. Because Aegis fails to offer a modicum of factual averment that Plaintiffs' patent infringement suit is objectively baseless, its counterclaim for sham litigation should be dismissed.

C. Aegis Fails to Plead Any Facts that Plaintiffs' Brought Their Lawsuit With a Subjective Motivation to Interfere Directly With the Business Relationships of a Competitor

Aegis failed to plead that Plaintiffs' suit is objectively baseless; therefore, the inquiry should end there. Even if, for purposes of this Motion, Aegis satisfied the "objectively baseless" component, it failed to properly allege facts that demonstrate Plaintiffs filed this action "with a subjective motivation to interfere directly with the business relationships of a competitor." *Andrx Pharms., Inc. v. Elan Corp., Inc.*, 421 F.3d 1227, 1233-34 (11th Cir. 2005). The sham litigation exception to antitrust immunity is based on a litigant's motive to harm one's competitors by the simple fact of the institution of a lawsuit. *GTE Data Services, Inc. v. Electronic Data Systems Corp.*, 717 F.Supp. 1487, 1490 (M.D. Fla. 1989). "Without a proper allegation of such a motive and ***well-pleaded facts to infer such a motive***, a claim under the sham exception is fatally defective." *Id.* (emphasis added) (quoting *City of Gainsville v. Florida Power & Light Co.*, 488 F.Supp. 1258, 1266 (S.D. Fla. 1980).

Where, as here, a complaint, "challenges a single suit rather than a pattern [of suits], . . . a finding of sham requires not only that the suit is baseless, but also that it has other characteristics of grave abuse, such as being coupled with actions or effects ***external*** to the suit that themselves

are anticompetitive." *Boulware v. Nevada*, 960 F.2d 793, 797-98 (9th Cir. 1992) (internal quotations omitted and emphasis added); *see also McGuire Oil Co. v. Mapco, Inc.*, 958 F.2d 1552, 1561 n.12 (11th Cir. 1992) (explaining on summary judgment that the defendant failed to satisfy the second prong of the sham litigation test because it "presented no facts to suggest that plaintiff's lawsuit was brought as part of an anticompetitive plan *external to the underlying litigation.*") (emphasis in original); *GTE Data Services,* 717 F.Supp. at 1491 (holding that plaintiff sufficiently pleaded motive to satisfy second prong of sham litigation test where it alleged (1) there was a limited number of persons qualified to perform required services, (2) the defendant employed the vast majority of qualified personnel, (3) the defendant required its employees to sign unenforceable non-compete agreements, and (4) the defendant, in bad faith, and with knowledge that the non-compete agreements were unenforceable, sued or threatened to sue its former employees to restrain competition.).

Aegis simply employs labels, conclusions, and formulaic recitations of the elements of the cause of action with no underlying factual bases.

> 37. Amertiox and UDT have initiated and maintained this objectively baseless "sham litigation" against its competitor, Aegis, without regard to the merit of the litigation, in order to exploit the judicial process (as opposed to the process) as an anticompetitive weapon.

Noticeably absent from Aegis' counterclaim are ***any*** facts of bad faith, motive, or intent. Its arguments to the contrary are unsupported. *First,* Aegis contends that it made "specific allegations that evidence Ameritox's motivation to interfere with its business relationship." (Response at 9; Counterclaim ¶ 11). Aegis charges, in part, that Ameritox "agents, employees and/or sales representatives" made "false and/or misleading representations" in violation of the Lanham Act:

- "They [Aegis] copied us."
- "They [Aegis] stole our business model."
- "Aegis is 'doing what we [Amertiox] are doing, but not as well as we give you much more usable information."
- "Aegis is not giving enough information in their report."
- "Aegis doesn't do what the Physician needs. We [Ameritox] give you information that can tell whether or not your patient is really complaint."

(Response at 9; Counterclaim ¶ 11). But, claims that allege false representation under the Lanham Act "are subject to the heightened pleading requirement of Fed.R.Civ.P. 9(b)." *Cardionet, Inc. v. Lifewatch Corp.*, 2008 WL 567031, *2 (N.D. Ill. Feb. 27, 2008). Aegis failed to identify the time, place, and person responsible for making each statement; therefore, Aegis' unfounded allegations cannot be used as "evidence" that Ameritox filed this case solely to interfere with Aegis' business. *See In re Eagle Bldg. Technologies, Security Litigation*, 221 F.R.D. 582, 586 (S.D. Fla. 2004) (discussing Rule 9(b) pleading requirements). *Second*, Aegis makes much of the fact that "Ameritox has admitted that they are in direct competition with Aegis." (Response at 8). "[I]t is axiomatic that actions taken with an anti-competitive purpose or intent remain insulated from antitrust liability under the *Noerr-Pennington* doctrine." *McGuire*, 958 F.2d at 1560. Thus, the filing of a lawsuit against a competitor is not enough to plead (or prove) sham litigation. If Aegis were correct, then the mere filing of a lawsuit against a competitor would potentially subject a party to an anti-trust counterclaim every time. There is ***no*** authority supporting such a proposition.

D. Aegis' Counterclaim for Patent Misuse Must be Dismissed for Failure to State a Claim

Finally, the Court should dismiss Aegis' counterclaim for patent misuse. Aegis fails to provide any legal support for the proposition that the sufficiency of a pre-filing investigation is the proper basis of a patent misuse claim. The cases cited by Aegis deal exclusively with sanctions under Rule 11; therefore, they are inapposite. Furthermore, Aegis fails to allege any fact that Plaintiffs "knew" or "should have known" that Aegis' services do not infringe the patents-in-suit. *See Takeda Chemical Indus., Ltd. v. Alphapharm Pty., Ltd.*, 2004 WL 1872707, * 1 (S.D.N.Y. Aug. 19, 2004) (striking affirmative defense of patent misuse because defendant merely parroted element of the claim without alleging even general facts in support).

Conclusion

WHEREFORE, Plaintiffs respectfully request that this Court enter an order dismissing Aegis' Sherman Anti-trust Act Sham Litigation and Patent Misuse counterclaims.

Dated: April 25, 2008

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CERTIFICATE OF SERVICE

I hereby certify that on April 25, 2008, I electronically filed the foregoing document with the Clerk or the Court using CM/ECF. I also certify that the foregoing document is being served on all counsel of record on the below Service List in the manner specified, either via transmission of Notices of Electronic Filing generated by CM/ECF or in some other authorized manner for those counsel or parties who are not authorized to receive electronically Notices of Electronic Filing.

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SERVICE LIST
Ameritox Ltd. and U.D. Testing, Inc. v. Aegis Sciences Corp.
Case No. 07-80498
United States District Court, Southern District of Florida

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EXHIBIT F

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

CASE NO. 07-80498-CIV-MARRA/JOHNSON

AMERITOX, LTD., and
U.D. TESTING, INC.,

Plaintiffs,

vs.

AEGIS SERVICES CORP.,

Defendant.
_____/

OPINION AND ORDER

This cause is before the Court upon Plaintiffs' Motion to Dismiss Defendant's Sherman Anti-Trust Act Sham Litigation and Patent Misuse Claims (DE 37) and Plaintiffs' Motion for Leave to File Second Amended Complaint (DE 52). The Court has carefully considered the motions and is otherwise fully advised in the premises.

A. Motion for Leave to File Second Amended Complaint

On June 11, 2007, Plaintiffs brought a two-count Complaint for patent infringement against Defendant. On December 21, 2007, within the time frame allowed for amendment of pleadings by this Court's September 28, 2007 Scheduling Order (DE 20), Plaintiff moved to amend that Complaint to add claims for a violation of the Florida Deceptive and Unfair Trade Practices Act, Tortious Interference with Business Relationship, Fraudulent Misrepresentation and False Marking. (DE 24.) Over the objection of Defendant, the Court permitted Plaintiffs to amend the complaint. (DE 28.) On May 8, 2008, Plaintiffs sought leave to amend their complaint again in order to dismiss their claims of patent infringement without prejudice and to

add a claim for false advertising under the Lanham Act. In making their application, Plaintiffs acknowledge that the December 21, 2007 deadline for amendment has passed and assert that good cause exists under Rule 16(b) of the Federal Rules of Civil Procedure to allow amendment at this late date. According to Plaintiffs, they did not learn of Defendant's non-infringement until a settlement meeting on March 20, 2008. (DE 52 at 7.) Nor did Plaintiffs know that Defendant's product did not contain certain advertised features that are now the basis for Plaintiffs' proposed Lanham Act claim. (DE 52 at 6.)

Defendant vigorously opposes this amendment, noting that the Lanham Act claim should have been brought in either the original complaint or the first amended complaint. In addition, Defendant states that the "gravamen of this action has always been patent infringement" and that the patent infringement claims were always "baseless." (DE 53 at 1-2.) Defendant also contends that Plaintiffs failed to adequately investigate their claims prior to filing this lawsuit. (DE 53 at 14-15.)

In ruling on Plaintiffs' application, the Court begins by examining Rule 15(a) of the Federal Rules of Civil Procedure. That rule provides that a party may amend the party's pleading "by leave of court or by written consent of the adverse party" and that "leave shall be freely given when justice so requires." Fed. R. Civ. P. 15(a). In construing Rule 15(a), the Supreme Court has held that there must be a substantial reason to deny amendment. Foman v. Davis, 371 U.S. 178, 182 (1962).

More than twenty years after the Supreme Court's decision in Foman, the 1983 Amendments to the Federal Rules of Civil Procedure altered Rule 16 to contain a provision restricting the timing of amendments. Fed. R. Civ. P. 16(b). Under Rule 16, district courts are

required to "enter a scheduling order that limits the time to . . . join other parties and to amend the pleadings . . . ." Id. The scheduling order "control[s] the subsequent course of the action" unless modified by the court. Fed. R. Civ. P. 16(e). As noted by one court, the scheduling order "is not a frivolous piece of paper, idly entered, which can be cavalierly disregarded by counsel without peril." Gestetner Corp. v. Case Equipment Co., 108 F.R.D. 138, 141 (D. Me. 1985).

A scheduling order may be modified only upon a showing of good cause. See Watkins v. Farmers & Merchant Bank, 237 Fed App'x 591, 593 (11th Cir. 2007); Sosa v. Airprint Systems, Inc., 133 F.3d 1417, 1418 (11th Cir. 1998). This good cause standard precludes modification unless the schedule cannot "be met despite the diligence of the party seeking the extension." Fed. R. Civ. P. 16 advisory committee's notes, cited in Sosa, 133 F.3d at 1418. In other words, good cause exists when evidence supporting the proposed amendment would not have been discovered in the exercise of reasonable diligence until after the amendment deadline had passed. See Forstmann v. Culp, 114 F.R.D. 83, 85-86 (M.D.N.C. 1987). Moreover, even if the opposing party would not be prejudiced by the modification of a scheduling order, good cause is not shown if the amendment could have been timely made. See Hayes v. Rule, No. 1:03CV1196, 2005 WL 2136946, at *4 (M.D.N.C. August 19, 2005).

It has been held that a Court's evaluation of good cause is more stringent than its inquiry into the propriety of amendment under the more liberal Rule 15. See Sosa, 133 F.3d at 1418; see also Forstmann, 114 F.R.D. at 85. Thus, even if Plaintiffs could demonstrate that the amendment is proper under Rule 15, the Court must first determine whether Plaintiffs have shown good cause under Rule 16(b) because Plaintiffs' Motion was filed after the scheduling order's deadline. See Sosa,133 F.3d at 1419. In other words, the likelihood of obtaining permission to amend

diminishes drastically after the deadline for amendments contained in the scheduling order expires.

After careful review, the Court finds that Plaintiffs have not made a showing of good cause to amend the complaint at this late date, i.e., nearly five months after the deadline set forth in the scheduling order. The evidence to which Plaintiffs point in support of their amendment should have been known to Plaintiffs prior to the deadline for amendment of pleadings, or at the very least earlier than May 8, 2008, the date they filed the instant motion. Although Plaintiffs claim that Defendant was not forthcoming with discovery, Plaintiffs did not act in a timely fashion to obtain discovery. In fact, a review of Magistrate Judge Johnson's order denying Plaintiffs' motion to compel discovery reveals that Plaintiffs did not timely move to compel adequate responses to discovery requests.[1] (DE 49).

Moreover, the Court rejects Plaintiffs' attempt to blame Defendant for their own failure to recognize that Defendant's product was different from Plaintiffs. For example, Plaintiffs argue that Defendant did not admit that it performed traditional drug testing, as opposed to the patented drug testing performed by Plaintiffs, and that based on Defendant's advertisement for its product, Plaintiffs were led to believe that Defendant's product infringed Plaintiffs' patent. (DE 52 at 5-6.) In other words, Plaintiffs seek to convert their non-viable patent claim into a Lanham act claim by contending that they were misled by Defendant's advertisement to believe that Plaintiffs' patent was infringed. The Court, however, finds these statements to be indicative of Plaintiffs' failure to gain a full understanding of Defendant's product by the deadline to amend

[1] Initially, Plaintiffs complained to the Magistrate Judge that Defendant did not timely file answers to interrogatories and responses to the request to produce. Plaintiffs, however, later admitted that Defendant did submit those responses. (DE 49.)

the pleadings. This hardly meets the standard for good cause. Lastly, the Court notes that it has been generous to Plaintiffs with respect to amendment. The Court permitted the prior amendment, an amendment which greatly expanded this case beyond the original patent infringement action. Thus, for these reasons, the Court denies Plaintiffs' Motion for Leave to File Second Amended Complaint.

B. Motion to Dismiss Defendant's Sherman Anti-Trust Act Sham Litigation and Patent Misuse Claims

In response to Plaintiffs' First Amended Complaint, Defendant filed its Answer to First Amended Complaint and Counterclaim (DE 30). Defendant's counterclaims are: non-infringement of the '788 patent (count one); invalidity of the '788 patent (count two); non-infringement of the '136 patent (count three); invalidity of the '136 patent (count four); commercial disparagement under the Lanham Act (count five); unfair competition (count six); violation of Florida Deceptive and Unfair Trade Practices Act (count seven); a Sham Litigation claim pursuant to the Sherman Anti-Trust Act (count eight) and patent misuse (count nine).

The allegations relating to all of these counterclaims include assertions that Plaintiffs and Defendant are "direct competitors in the drug testing industry." (Counterclaim ¶ 6.) Defendant uses a "substantially dissimilar scientifically validated and recognized method" in contrast to Plaintiffs' "junk science" method. (Counterclaim ¶ ¶ 7-8.) Plaintiffs have sought to "gain an unfair, improper and unlawful advantage in its competition with [Defendant] in the marketplace" by "engag[ing] in a concerted effort to disparage, and harm the reputation of [Defendant]." (Counterclaim ¶ 9.) To that end, Plaintiffs have "willfully made false and/or misleading representations of fact regarding the nature and qualities of the services and commercial activities

of [Defendant], including false accusations of unethical and unlawful conduct, false and misleading statements regarding the drug testing services provided by [Defendant], and the false accusation that [Defendant] uses the same [ ] science employed by [Plaintiffs] in providing its drug monitoring services." (Counterclaim ¶ 10.) For example, Plaintiffs have told prospective clients of Defendant that Defendant "copied us," "stole our business model," "is doing what [Plaintiffs do] but not as well," and that Defendant does not give "enough information in [its] report," or "do what the physician needs." (Counterclaim ¶ 11.)

Plaintiffs seek dismissal of the Sherman Anti-Trust Act Sham Litigation and patent misuse claims. The Sherman Anti-Trust Act Sham Litigation claim states that Plaintiffs "have initiated and maintained this objectively baseless 'sham litigation' against its competitor, [Defendant], without regard to the merits of this litigation, in order to exploit the judicial processes (as opposed to the outcome of the processes) as an anticompetitive weapon." (Counterclaim ¶ 37.) With respect to the patent misuse claim, Defendant alleges that it is "entitled to a declaration that the patents in suit are void and unenforceable because of [Plaintiffs'] patent misuse in commencing litigation against [Defendant] without undertaking the necessary objective pre-filing investigation to determine whether the accused products or services infringed the claims of the patents in suit and then continuing this litigation knowing that [Defendant] did infringe the claims of the patent in suit." (Counterclaim ¶ 42.)

In moving for dismissal, Plaintiffs argue that the alleged facts are simply formulaic recitations of the elements of the causes of action. With respect to the sham litigation claim, Plaintiffs assert that the alleged facts do not show that Plaintiffs' lawsuit is "objectively baseless" or was brought with the "subjective motivation to interfere directly with the business relationship

of a competitor." (DE 37 at 5.) In response, Defendant provides additional factual context in support of its contention that Plaintiffs' patent infringement claims were objectively baseless. (DE 45 at 4-8.) With respect to the patent misuse claim, Plaintiffs contend that, even assuming the facts pled are true, none of those facts sufficiently plead that claim. (DE 37 at 1-2.)

1. Legal Standard

Rule 8(a) of the Federal Rules of Civil Procedure requires "a short and plain statement of the claims" that "will give the defendant fair notice of what the plaintiff's claim is and the ground upon which it rests." Fed.R.Civ.P. 8(a). The Supreme Court has held that "[w]hile a complaint attacked by a Rule 12(b)(6) motion to dismiss does not need detailed factual allegations, a plaintiff's obligation to provide the 'grounds' of his 'entitlement to relief' requires more than labels and conclusions, and a formulaic recitation of the elements of a cause of action will not do. Factual allegations must be enough to raise a right to relief above the speculative level." Bell Atlantic Corp. v. Twombly, 127 S.Ct. 1955, 1964-65 (2007) (internal citations omitted). When considering a motion to dismiss, the Court must accept all of the plaintiff's allegations as true in determining whether a plaintiff has stated a claim for which relief could be granted. Hishon v. King & Spalding, 467 U.S. 69, 73 (1984).

2. Sherman Anti-Trust Act Sham Litigation

The Sherman Anti-Trust Act proscribes acts that restrain trade. See 15 U.S.C. § § 1-2; Andrx Pharmaceuticals, Inc. v. Elan Corp., PLC, 421 F.3d 1227, 1233 (11th Cir. 2005). Notwithstanding the reach of that Act, the Noerr-Pennington doctrine creates immunity from Sherman Act liability when a party brings litigation that results in an anticompetitive outcome. Andrx, 421 F.3d at 1233. However, an exception to Noerr-Pennington exists where a party

engages in "sham litigation." Id. A party asserting that Noerr-Pennington immunity should not apply must establish the following: "(1) the lawsuit is objectively baseless in the sense that no reasonable litigant could realistically expect success on the merits; and (2) the party bringing the allegedly baseless suit did so with a subjective motivation to interfere directly with the business relationships of a competitor." Id. at 1234 quoting Professional Real Estate Investors, Inc. v. Columbia Pictures Industries, Inc., 508 U.S. 49, 60-61 (1993) (internal quotation marks and emphasis omitted). In demonstrating that a party brought a lawsuit as part of an anticompetitive plan external to the underlying litigation, it is necessary to make a showing of bad faith. See Professional Real Estate Investors, 508 U.S. at 60; Porous Media Corp.v. Pall Corp., 186 F.3d 1077, 1080 n.4 (8th Cir. 1999); C. R. Bard, Inc. v. M3 Systems, Inc., 157 F.3d 1340, 1368-69 (Fed. Cir. 1998); McGuire Oil Co. v. Mapco, Inc., 958 F.2d 1552, 1561 n.12 (11th Cir. 1992). Bad faith can include reckless conduct as well as deliberately and knowingly engaging in wrongdoing, fraud or misconduct. Amlong & Amlong P.A. v. Denny's, Inc., 500 F.3d 1230, 1239-41 & n.1 (11th Cir. 2007) (discussing bad faith in the context of sanctions against an attorney); Barnes v. Dalton, 158 F.3d 1212, 1214 (11th Cir. 1998) (same) see also Black's Law Dictionary (8th ed. 2004) (defining bad faith as "dishonesty of belief or purpose").

With respect to the first prong of this test, Plaintiffs correctly note that the counterclaim fails to provide any factual basis to support this element of the cause of action. The facts supporting the counterclaim (Counterclaim ¶ 9) and the counterclaim (Counterclaim ¶ 37) itself merely recites the legal standard. However, Defendant's response to the motion provides numerous facts which explain notable differences between Plaintiffs and Defendant's product. For example, Defendant states that it engages in "traditional urine testing" in contrast to

"therapeutic drug monitoring,"and that it "does not use the 'typical morning void' as its standard for comparison of specific gravity" but a "different standard reflecting an 'ideal' population." (DE 45 at 4-8.) Some of these facts are supported by declarations, but are not in the pleading. Therefore, the Court cannot consider those facts. See Grossman v. Nationsbank, N.A., 225 F.3d 1228, 1231 (11th Cir. 2000) (on a motion to dismiss, the Court cannot consider evidence outside of the pleadings). However, Defendant can amend this counterclaim to include facts that would demonstrate that Plaintiffs' patent infringement action was objectively baseless.

With respect to the second prong, Plaintiffs argue that Defendant's "facts fail to state anything that, if taken as true, could support the contention that Plaintiffs are using this lawsuit to interfere directly with [Defendant's] business relationships." (DE 37 at 8.) Defendant does, however, identify various false statements allegedly made to prospective clients that were made "willfully." (Counterclaim ¶ ¶ 10-11.) Thus, Plaintiffs' charge that Defendant's counterclaim is devoid of any facts evidencing bad faith (DE 51 at 7) can be rejected.[2] Likewise, Plaintiffs' claim that Defendant failed to plead facts that Plaintiffs' lawsuit was brought as part of anticompetitive plan external to the underlying litigation is rejected. (DE 51 at 6-7.) First, Defendant did plead that Plaintiffs sought to "gain an unfair, improper and unlawful advantage in

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[2] The Court is puzzled by Plaintiffs' reference to the Lanham Act and the heightened pleading standards they claim applicable to that act. (DE 51 at 7-8.) Plaintiffs did not move to dismiss Defendant's Lanham Act counterclaim. In any event, to the extent Plaintiffs are seeking the application of a heightened pleading standard to allegations of sham litigation, the Court rejects that application. See Andrx, 421 F.3d at 1234-35 (applying Rule 8(a) notice pleading standard to antitrust violations); St. Joseph Hosp., Inc. v. Hospital Corp. of America, 795 F.2d 948, 953-54 (11th Cir. 1986) (applying Rule 8 to sham litigation actions); SecurityPoint Media, LLC v. Adason Group LLC, No. 8:07-cv-444-T-24TGW, 2007 WL 2298024, * 5 (M.D. Fla. Aug. 7, 2007) (declining to impose a heightened pleading standard to allegations of sham litigation).

its competition with [Defendant] in the marketplace" by "engag[ing] in a concerted effort to disparage, and harm the reputation of [Defendant]" and "willfully made false and/or misleading representations of fact regarding the nature and qualities of the services and commercial activities of [Defendant], including false accusations of unethical and unlawful conduct, false and misleading statements regarding the drug testing services provided by [Defendant], and the false accusation that [Defendant] uses the same junk science employed [Plaintiffs] in providing its drug monitoring services." (Counterclaim ¶ ¶ 9-10.) At the pleading stage, the Court finds these allegations sufficient. Second, Plaintiffs' reliance on McGuire Oil is unavailing. (DE 51 at 7.) That case addressed the evidentiary burden of a sham litigation claim in the summary judgment context, finding there was no record evidence to suggest that the party bringing the underlying lawsuit did not "honestly believe that their claims . . . were meritorious." McGuire Oil, 958 F.2d at 1561 n.12. In other words, McGuire Oil does nothing to support Plaintiffs' objections at this stage of the proceedings. As such, the Court rejects Plaintiffs' argument that Defendant did not adequately plead that Plaintiffs brought their suit with a subjective motivation to interfere directly with the business relationships of a competitor.

3. Patent Misuse

Plaintiffs move to dismiss Defendant's counterclaim of patent misuse. Although Plaintiffs attack the manner in which this counterclaim was pled, the Court finds that these arguments fail to raise the most compelling basis to dismiss this counterclaim; namely, patent misuse is an affirmative defense to the accusation of patent infringement. Virginia Panel Corp. v. MAC Panel Co., 133 F.3d 860 (Fed. Cir. 1997). In other words, the proper mechanism to

assert patent misuse is to plead it is an affirmative defense, which Defendant did.[3] (Affirmative Defenses ¶ 8.) Therefore, the Court dismisses Defendant's counterclaim of patent misuse; however, Defendant is entitled to pursue the affirmative defense of patent misuse.

C. Conclusion

Accordingly, it is hereby **ORDERED AND ADJUDGED** that Plaintiffs' Motion to Dismiss Defendant's Sherman Anti-Trust Act Sham Litigation and Patent Misuse Claims (DE 37) is **GRANTED** in part and **DENIED** in part. Defendant is granted leave to amend the Sherman Anti-Trust Act counterclaim according to the directives set forth in this Order. The patent misuse counterclaim is dismissed. Plaintiffs' Motion for Leave to File Second Amended Complaint (DE 52) is **DENIED**.

DONE AND ORDERED in Chambers at West Palm Beach, Palm Beach County, Florida, this 9th day of July 2008.

KENNETH A. MARRA
United States District Judge

[3] The Court notes that this defense derives from the equitable doctrine of unclean hands and "relates generally to the use of patent rights to obtain or coerce an unfair commercial advantage." C.R. Baird, Inc. v. M3 Systems, Inc., 157 F.3d at 1372.

EXHIBIT G

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA
WEST PALM BEACH DIVISION

AMERITOX, LTD., and
U.D. TESTING, INC.,

Plaintiffs,

v.

AEGIS SCIENCES CORP.,

Defendant.
_____/

Case No. 07-80498

J. Marra

STIPULATED PROTECTIVE ORDER

WHEREAS, the Parties, Plaintiffs Ameritox, Ltd. and U.D. Testing, Inc. and Defendant Aegis Sciences Corp. (hereinafter "Parties"), and non-Parties may, during the course of this action, be required to disclose trade secrets and other confidential research, development, marketing, or proprietary commercial information within the meaning of Rule 26(c) of the Federal Rules of Civil Procedure; and

WHEREAS, the Parties, through counsel, have moved for entry of this Protective Order pursuant to Rule 26(c) to prevent unnecessary disclosure or dissemination of such confidential information;

IT IS HEREBY ORDERED that the following provisions of this Protective Order regarding confidentiality (hereinafter "Order") shall govern, *nunc pro tunc*, and control the disclosure, dissemination, and use of information in this action.

1. This Order shall govern the production, use, and disclosure of confidential documents and information produced, used, or disclosed in connection with these actions and designated in accordance with this Order. Any Party or non-Party disclosing information

(hereinafter "Disclosing Party") may designate information or documents produced, used, or disclosed in connection with these actions as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" and subject to the protections and requirements of this Order, if so designated in writing to each Party, by stamping the legend "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" on the documents or information prior to production, or orally if recorded as part of a deposition or court record, pursuant to the terms of this Order.

2. Any Disclosing Party may designate any document, material, or information as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL." In designating information and materials as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" counsel for a Disclosing Party will make such designation only as to that information that he or she in good faith believes to be "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" as defined in Paragraph 2(a) or 2(b) of this Order.

a. "CONFIDENTIAL" means trade secrets, other confidential, non-public and proprietary technical information, including, research, or development information, unpublished patent applications, commercial, financial, budgeting and/or accounting information, information about existing customers, marketing studies, performance and projections, business strategies, decisions and/or negotiations, personnel compensation, evaluations and other employment information, and confidential and proprietary information about affiliates, parents, subsidiaries and third Parties with whom the Parties to this action have had business relationships which a Disclosing Party in good faith so designates because of its view that the information or any information derived therefrom contains or reflects trade secrets, or other confidential research, development, or commercial information. The "CONFIDENTIAL" category shall be invoked by a Disclosing Party only relative to documents

or categories of documents that contain confidential information that legitimately falls within the definition of protectable documents under Fed. R. Civ. P. 26(c).

b. "HIGHLY CONFIDENTIAL" means only confidential information and documents as defined in 2(a) which warrant further protection because the information, if disclosed to a business competitor, would tend to damage the Disclosing Party's competitive position.

3. To the extent the Disclosing Party is a non-Party to the current litigation, counsel for the Parties to the current litigation may change the designation of a document under the circumstances of Paragraph 3(a) and 3(b) of this Order.

a. If a non-Party produces information designated as "CONFIDENTIAL" or produces information without any confidentiality designation, a Party has the right to change such designation to the extent the designated, or non-designated, information at issue contains information that the Party in good faith deems "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" to that Party as defined by Paragraph 2. Any re-designation by a Party will be given full effect of protection under this Order.

b. If a non-Party re-designates information containing a Party's "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" information, a Party has the right to change such designation to the extent the re-designated document at issue contains information that the Party in good faith deems "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" to that Party as defined by Paragraph 2. A non-Party or Party may challenge the changed designation. Any challenge to such re-designation must follow the requirements of Paragraph 7 of this Order.

4. In the case of a document, a designation of "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" shall be accomplished by marking the document with the legend

"CONFIDENTIAL" or "HIGHLY CONFIDENTIAL." Marking the cover of a multi-page document shall not designate all pages of the document confidential; rather, each page containing confidential information must be separately marked. As to those documents that are produced for examination for the purposes of allowing opposing counsel to determine which of those documents opposing counsel desires copies, those documents shall be treated as "HIGHLY CONFIDENTIAL" pursuant to this Order, whether or not marked, until copies of the documents are requested and produced, at which time the produced documents and information therein shall be held pursuant to this Order based upon the designation, if any, marked upon the documents by the Disclosing Party.

5. Information conveyed or discussed in testimony at a deposition or a court hearing shall be subject to this Order provided it is designated "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" orally or in writing either at or after the time the testimony is given. During such time as any information or documents designated "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" are disclosed in a deposition or court hearing, any Party shall have the right to exclude from attendance at the deposition or court hearing any person who is not entitled to receive such information or documents pursuant to this Order. Unless counsel for a Party states otherwise on the record, the entire deposition transcript for each deponent in this action and the information contained therein is to be treated as "HIGHLY CONFIDENTIAL" for a period of time not to exceed 30 days after the Party receives a copy of the deposition transcript, during which time the Party may designate, in writing, specific portions of the transcript "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" as appropriate. If the Party fails to designate in writing any portions of the transcript as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" within the 30 day period, the other Parties shall be permitted to use the

transcript and the information contained therein with no restrictions of confidentiality subject to the provisions of paragraph 6 below.

6. Subject to the provisions of Paragraphs 2, 3 and 4, the failure to designate information or documents as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" in accordance with this Order and the failure to object to such a designation shall not preclude a Party at a later time from subsequently designating or objecting to the designation of such information or documents as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL." The Parties understand and acknowledge that failure of a Party to designate information or documents as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" relieves the receiving Party of obligations of confidentiality until such a designation is made, except as otherwise provided herein.

7. A Party that objects to the designation of any document or information as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" shall provide written notice of the objection to the Disclosing Party or, if the Disclosing Party is a non-party, to the other Party. The notice shall state with specificity the document objected to and the basis for the objection. If the dispute cannot be resolved, the objecting Party may move the Court requesting that the document(s) in question be redesignated. If such motion is brought by the objecting Party, the Disclosing Party shall bear the burden of establishing the confidentiality of the document(s) in question. No Party shall be under any obligation to object to any designation of confidentiality at the time such designation is made, or any time thereafter. No Party shall, by failure to object, be found to have acquiesced or agreed to such designation or be barred from objecting to such designation at any time thereafter.

8. Other than by the Disclosing Party, and as further limited by Paragraph 10 below, any information or document designated as "CONFIDENTIAL" shall be used solely in

connection with the action and shall not be used in any other manner by a receiving Party. Any such designated information or documents shall not be disclosed to anyone other than:

a. the Court and Court personnel;

b. court reporters taking testimony in these actions and their necessary stenographic, videographic, and clerical personnel;

c. outside counsel of record for the Parties and outside counsel's employees including internal and external document vendors;

d. no more than five (5) designated employees of each Party, as agreed upon by counsel solely for purposes of the Action, who shall, prior to receiving such disclosure, be furnished with a copy of this Order and shall execute a Declaration in the form of Exhibit A attached hereto, confirming that he/she has read and understands the provisions of this Order and agrees to be bound hereby ("Designated Employees"). The access of Designated Employees to documents designated "CONFIDENTIAL" shall be limited to the opposing Party's information contained within deposition transcripts and exhibits thereto, written discovery, and documents filed with the Court, including exhibits thereto.

e. experts, investigators, jury consultants, and mock jury members that are not presently employees of a Party, provided, however, that before any such person other than a mock jury member is shown or receives any information or document designated as "CONFIDENTIAL," he or she must execute a Declaration in the form of Exhibit A attached hereto and the procedures of Paragraph 11 shall be followed;

f. persons testifying in depositions or court proceedings (including, without limitation, persons preparing to testify in such depositions or court proceedings) to the extent the

"CONFIDENTIAL" document or information was authored by, addressed to, or received by the person or Party testifying; and

g. such other persons as the Parties may designate in writing by stipulation or orally agree upon on the record at a deposition in these actions, provided, however, that before such person is shown or receives any information or document designated as "CONFIDENTIAL" he or she must (1) execute a Declaration in the form of Exhibit A attached hereto or (2) agree orally on the record at a deposition in these actions to be bound by the terms of this Order, and further provided that any documents designated as "CONFIDENTIAL" shall not be left in the possession of the person subject to this subparagraph "g", except as may be required by Fed. R. Civ. P. 30 or unless the person otherwise qualifies for access to such documents pursuant to this Order.

9. Other than by the Disclosing Party and as limited by Paragraph 10 below, any information or document designated as "HIGHLY CONFIDENTIAL" shall be used solely in connection with the action and shall not be used in any other manner by a receiving Party. Any such designated information or documents shall not be disclosed to anyone other than:

a. the Court and Court personnel;

b. court reporters taking testimony in these actions and their necessary stenographic, videographic, and clerical personnel;

c. outside counsel of record for the Parties and outside counsel's employees including internal and external document vendors;

d. experts, jury consultants, and mock jury members that are not presently employees of a Party, provided, however, that before any such person other than a mock jury member is shown or receives any information or document designated as "HIGHLY

CONFIDENTIAL" he or she must execute a Declaration in the form of Exhibit A attached hereto and the procedures of Paragraph 11 shall be followed;

e. persons testifying in depositions or court proceedings (including, without limitation, persons preparing to testify in such depositions or court proceedings) to the extent the "HIGHLY CONFIDENTIAL" document or information was authored by, addressed to, or received by the person or Party testifying;

f. for documents produced by either Party in this action, and subject to subparagraph 9(g) below, such other persons as the Parties may designate in writing by stipulation or orally agree upon on the record at a deposition in these actions, provided, however, that before such person is shown or receives any information or document designated as "HIGHLY CONFIDENTIAL" he or she must (1) execute a Declaration in the form of Exhibit A attached hereto or (2) agree orally on the record at a deposition in these actions to be bound by the terms of this Order, and further provided that any documents designated as "HIGHLY CONFIDENTIAL" shall not be left in the possession of the person subject to this subparagraph "f", except as may be required by Fed. R. Civ. P. 30 or unless the person otherwise qualifies for access to such documents pursuant to this Order.

g. for documents produced by a non-Party to this action, such other persons as the non-Party may designate in writing by stipulation or orally agree upon on the record at a deposition in these actions, provided, however, that before such person is shown or receives any information or document designated as "HIGHLY CONFIDENTIAL" he or she must (1) execute a Declaration in the form of Exhibit A attached hereto or (2) agree orally on the record at a deposition in these actions to be bound by the terms of this Order, and further provided that any documents designated as "HIGHLY CONFIDENTIAL" shall not be left in the possession of the

person subject to this subparagraph "g", except as may be required by Fed. R. Civ. P. 30 or unless the person otherwise qualifies for access to such documents pursuant to this Order.

10. The attorneys of record for each of the Parties shall retain the original, executed Declarations (in the form of Exhibit A hereto) that have been executed by that Party and/or its employees and that Party's witnesses, testifying experts, investigators, consultants, advisors, and jury consultants. It shall be sufficient for a testifying expert, investigator, consultant, advisor, and jury consultant to execute the Declaration on behalf of the members and employees of his or her firm; no additional Declarations are necessary from such members and employees. Prior to disclosure of any documents or information designated "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" to any experts, a copy of the executed Declaration shall be served upon opposing counsel via email and overnight delivery and, for non-Party documents or information designated by the non-Party as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL," upon the non-Party (with a copy of such person's curriculum vitae, a general statement of any prior or current relationship or connection with either Party, a list of all cases in which such person has been deposed or has testified as an expert, and a general statement as to the issues the expert is intended to opine upon attached). Opposing counsel and, if applicable, each non-Party, shall make any objections to the disclosure to the testifying expert in writing no later than five (5) business days from the date of receipt of the hard copy received via overnight delivery. No such disclosure shall occur until the objection is resolved or the Court grants a motion permitting the disclosure. The burden to file any such motion is on the Party that seeks to disclose documents or information designated "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" to a testifying expert. Any such objections to the disclosure must be in good faith and not interposed for purposes of delay or harassment. Except as permitted by Rule 26(b)(4)(B) of the Federal Rules

of Civil Procedure, the Parties agree that no written or oral discovery of consulting experts may be taken until and unless such expert is designated as a testifying expert.

11. Whenever any document designated as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" or any pleading, motion, memorandum, or other paper designated as containing "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" information is filed with the Court, such document or pleading, motion, memorandum, or other paper shall be filed under seal and shall display a bold heading on its first page in substantially the following form: "FILED UNDER SEAL SUBJECT TO PROTECTIVE ORDER." The Clerk of the Court is directed to maintain under seal only those documents and transcripts of deposition testimony filed in the Court in this litigation which have been designated, in whole or in part, as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" by a Party to this litigation. Such designation shall be readily visible and legible on at least the cover of each such document and/or transcript filed with the Court.

12. Unless otherwise permitted herein, within sixty (60) days after the final disposition of the action, including all appeals therefrom, all documents (originals and copies) designated as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" and all excerpts therefrom in the possession, custody, or control of Parties other than the Disclosing Party, and experts, investigators, advisors, or consultants shall be destroyed or returned to counsel for the Disclosing Party. Outside Counsel for Parties other than the Disclosing Party may retain one copy of each document, pleading, trial exhibit, deposition exhibit, work product, and transcript embodying documents or information designated as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" for archival purposes only, but shall destroy or return all additional copies of such documents, pleadings, trial exhibits, deposition exhibits, work product, and transcripts. Upon request, the

Parties and their counsel shall separately provide written certification to the Disclosing Party within sixty (60) days after the final disposition of these actions that the actions required by this paragraph have been completed.

13. The Court shall retain jurisdiction over the Parties for the purpose of ensuring compliance with this Order and granting such amendments, modifications, and additions to this Order and such other and further relief as may be necessary, and any Party may apply to the Court at any time for an amendment, modification, or addition to this Order. This Order shall survive the final disposition of the action by judgment, dismissal, settlement, or otherwise.

14. A Party in receipt of documents or information designated as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" hereunder who is required to disclose the document or information pursuant to any law, regulation, order, or rule of any governmental authority, shall give immediate advance notice within two (2) business days, to the extent possible, or, if not possible, shall give notice as soon as possible thereafter, of any such requested or actual disclosure in writing to the counsel of the other Parties to afford the Parties the opportunity to seek legal protection from or otherwise limit the disclosure of such information or documents.

15. In the event that anyone violates or threatens to violate the terms of this Order, the Parties agree that the aggrieved Party may apply immediately to obtain injunctive relief against any such violation or threatened violation, and in the event the aggrieved Party shall do so, the respondent, subject to the provisions of this Order, shall not employ as a defense thereto any claim that the aggrieved Party possesses an adequate remedy at law.

16. Neither this Order nor any stipulation therefore, nor any disclosure or use of information or documents, in whatever form, pursuant to this Order, shall be deemed an admission, waiver, or agreement by any Party that any information or documents designated as

"CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" hereunder is or is not a trade secret or confidential information for purposes of determining the merits of any claim or claims any Party may have against one another or a third Party. Neither this Order nor any stipulation therefore shall be deemed to expand the scope of discovery in these actions beyond the limits otherwise prescribed by law, nor to enlarge the scope of discovery to matters unrelated to these actions.

17. Inadvertent production of documents subject to work product immunity, the attorney-client privilege or any other privilege or immunity shall not constitute a waiver of the immunity or privilege; provided that the Disclosing Party notifies the receiving Party in writing via facsimile or email of such inadvertent production immediately upon learning of same. Such inadvertently produced documents, and all copies thereof, shall be returned to the Disclosing Party upon request within three (3) business days except that, if the receiving Party intends to request that the Court order the production of any such inadvertently produced documents, it may retain one copy of the document for such purpose and if so, notify the Disclosing Party promptly. The receiving Party must return such inadvertently produced documents if the receiving Party does not request such relief from the Court within five (5) business days or if the Court denies any such relief, whichever is longer, and no use may be made of such documents thereafter. Nothing in this Protective Order shall prevent the receiving Party from requesting that the Court order the production of any such inadvertently produced documents. Nothing in this Protective Order prevents any Party from petitioning the Court for return of later discovered, inadvertently produced documents that are subject to work product immunity or attorney-client privilege.

18. Nothing in the order shall be construed to affect the admissibility of any document, material, or information at any trial or hearing; any request for confidentiality,

closure, or sealing of any hearing or trial must be made to the judge then presiding over this action. A Party intending to introduce confidential information or documentation at any hearing or trial in this action will approach the bench for a ruling on how the information or documentation is to be treated.

IT IS SO ORDERED:

Date: SEPT. 24, 2007

United States District Judge

Respectfully Submitted,

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U.D. TESTING, INC.

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EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA
WEST PALM BEACH DIVISION

AMERITOX, LTD., and
U.D. TESTING, INC.,

Case No. 07-80498

Plaintiffs,

J. Marra

v.

AEGIS SCIENCES CORP.,

Defendant.
_____/

DECLARATION OF _____ (Name of Declarant)

I, _____, declare as follows:

1. My address is _____

_____.

2. If I am an expert, a copy of my curriculum vitae is attached.

3. My present employer is _____

_____.

4. My present occupation or job description is _____

_____.

5. I have received a copy of the Protective Order entered in these actions on _____

_____.

6. I have carefully read and understood the provisions of the Protective Order.

7. I will comply with all of the provisions of the Protective Order.

8. I will hold in confidence, not to disclose to anyone not designated in the Protective Order, and will use only for the purposes of assisting in the resolution of disputes between the Parties to these actions, any information or documents designated as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL."

9. I will return all documents designated as "CONFIDENTIAL" or "HIGHLY CONFIDENTIAL" that may come into my possession, and documents or things which I may prepare relating thereto, to counsel for the Party who disclosed or furnished such documents to me promptly upon the request of counsel for all Parties or, if applicable, upon the request of counsel by whom I have been retained, or upon the conclusion of these actions.

10. I hereby submit to the jurisdiction of this Court for the purposes of enforcement against me of the terms of the Protective Order and of the terms of this Declaration.

11. I declare under penalty of perjury that the foregoing is true and correct.

Executed on _____ in _____.

_____
(Signature)